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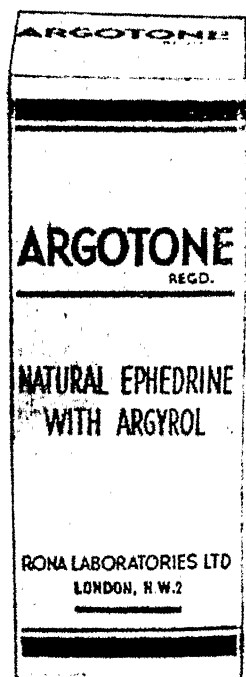
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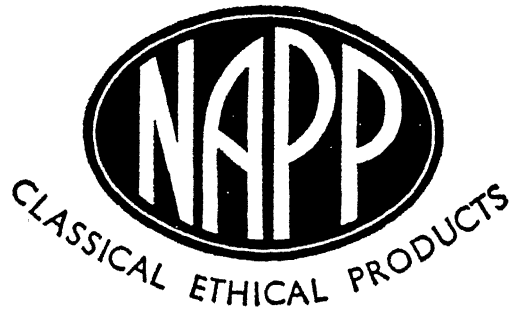
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1941-2**

Under the General Editorship of

**SIR HUMPHRY ROLLESTON, BT.
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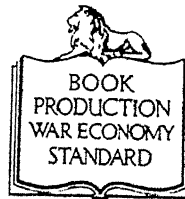
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CONTENTS

PART I—CRITICAL SURVEYS

GENERAL MEDICINE	- - - - -	PAGE 1
W. E. HUME, C.M.G., M.D., F.R.C.P. Emeritus Professor of Medicine, University of Durham; Consulting Physician, Royal Victoria Infirmary, Physician, General Hospital, Newcastle-on-Tyne		
GENERAL SURGERY	- - - - -	8
G. GREY TURNER, LL.D., D.Ch., M.S., F.R.C.S., F.R.A.C.S., F.A.C.S. Professor of Surgery, University of London; Director of Department of Surgery, British Postgraduate Medical School		
OBSTETRICS AND GYNAECOLOGY	- - - - -	16
JAMES YOUNG, D.S.O., M.D., F.R.C.S.Ed., F.R.C.O.G. Professor of Ob- stetrics and Gynaecology, University of London; Director of Department of Obstetrics and Gynaecology, British Postgraduate Medical School		
ALIMENTARY TRACT DISEASES	- - - - -	24
SIR ARTHUR HURST, D.M., F.R.C.P. Consulting Physician, Guy's Hospital		
AVIATION MEDICINE	- - - - -	29
AIR MARSHAL SIR HAROLD WHITTINGHAM, K.B.E., K.H.P., M.B., F.R.C.P., F.R.F.P.S., D.P.H., D.T.M. & H. Director-General Medical Services, Royal Air Force		
BLOOD TRANSFUSION IN RELATION TO TREATMENT OF SHOCK	- - - - -	38
F. A. KNOTT, M.D., F.R.C.P., D.P.H. Director, Bacteriological Department and Blood Transfusion Depot, Guy's Hospital		
CARDIOVASCULAR DISEASES	- - - - -	44
WILLIAM EVANS, M.D., F.R.C.P. Assistant Physician, Cardiac Department, London Hospital		
CHILDREN'S DISEASES	- - - - -	48
ALAN MONCRIEFF, M.D., F.R.C.P. Physician, Children's Department, Middlesex Hospital; Physician to Out-Patients, Hospital for Sick Children, Great Ormond Street; Paediatrician, Queen Charlotte's Maternity Hospital		
EAR, NOSE, AND THROAT DISEASES	- - - - -	52
LIONEL COLLEDGE, M.B., F.R.C.S. Surgeon, Golden Square Throat, Nose, and Ear Hospital; Aural Surgeon, West End Hospital for Nervous Diseases, London		
INFECTIONS, ACUTE	- - - - -	62
WILLIAM GUNN, M.B., M.R.C.P., D.P.H. Medical Superintendent, North Western Hospital, Hampstead		

LUNG AND PLEURA DISEASES	- - - - -	PAGE 71
JAMES L. LIVINGSTONE, M.D., F.R.C.P. Physician, King's College Hospital, London; Assistant Physician, Hospital for Consumption and Diseases of the Chest, Brompton; Physician, Chest Unit, Horton Emergency Hospital, E.M.S.		
MENTAL DISEASES	- - - - -	79
R. D. GILLESPIE, M.D., F.R.C.P., D.P.M. Physician in Charge, Department of Psychological Medicine, and Lecturer in Psychological Medicine, Medical School, Guy's Hospital; Wing Commander, R.A.F.V.R.		
NERVOUS DISEASES	- - - - -	88
J. PURDON MARTIN, M.D., F.R.C.P. Physician to Out-Patients, National Hospital for Nervous Diseases, Queen Square; Neurologist, British Postgraduate Medical School		
TROPICAL MEDICINE	- - - - -	96
SIR LEONARD ROGERS, K.C.S.I., LL.D., M.D., F.R.C.P., F.R.C.S., F.R.S. Late Physician, Hospital for Tropical Diseases, London		
VENEREAL DISEASES	- - - - -	102
BREVET-COLONEL L. W. HARRISON, D.S.O., M.B., Ch.B., F.R.C.P.Ed. Technical Adviser in Venereal Diseases, Ministry of Health; Consultant in Venereal Diseases, British Postgraduate Medical School, London		

PART II—DRUGS

RECENT DEVELOPMENTS IN DRUG THERAPY	- - - - -	111
W. J. DILLING, M.B., Ch.B. Professor of Pharmacology and General Therapeutics, University of Liverpool		

PART III—ABSTRACTS OF MEDICAL LITERATURE

ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES TO YELLOW FEVER	- - - - -	125
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INTRODUCTION

BY

THE GENERAL EDITOR

The general plan of the Annual Supplement to the BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE has been followed in this, the third Annual Supplement. As before, this volume is divided into three parts, which contain respectively a series of critical surveys of various branches of Medicine, a section dealing with new developments in drugs, and abstracts from current medical publications. I should like to acknowledge my indebtedness to the Publishing Editor, Dr. D. Hay Scott.

PART I—CRITICAL SURVEYS

This consists of a series of authoritative signed reviews dealing in general terms with the present position of some branches of medical science and practice, and indicating the possible future developments in these. The subjects dealt with in these critical surveys will vary from year to year according to the circumstances of medical progress. The Encyclopaedia is much indebted for the help given in these difficult times by the contributors of these surveys.

PART II—DRUGS

In this section new drugs, or modifications of old drugs, are discussed from their therapeutical and pharmacological aspects, and it is a pleasure to express high appreciation of Professor W. J. Dilling's help.

PART III—ABSTRACTS OF MEDICAL LITERATURE

This section brings together the essentials of a large number of papers published throughout the year ending June 30, 1941, by British, American, and other authors. As a result of the wide extent of the War the output of European journals and other medical publications has greatly diminished, but the supply from North America has so far been well maintained. Much care has been bestowed on the selection of these abstracts, which are arranged as far as possible on the same plan as that adopted in the parent Encyclopaedia. The material in this part contains the results and opinions of the authors of the abstracted papers, but it does not, of course, follow that all these will be finally accepted by the medical profession.

H. R.

ACKNOWLEDGMENTS

The Publishers acknowledge with thanks permission to include the following diagrams in the text:

On page 148, Anus Diseases, from the *Proceedings of the Royal Society of Medicine*, Vol. 34, p. 144 (Section of Proctology, p. 6), by permission of the Honorary Editors.

On page 271, Intestinal Obstruction, from the *British Medical Journal*, 1940, Vol. 2, p. 783.

On page 298, Lung Diseases: Blast Injuries, from the *British Medical Journal*, 1940, Vol. 2, p. 317.

GENERAL MEDICINE

By W. E. HUME, C.M.G., M.D., F.R.C.P.

EMERITUS PROFESSOR OF MEDICINE, UNIVERSITY OF DURHAM; CONSULTING PHYSICIAN,
ROYAL VICTORIA INFIRMARY, PHYSICIAN, GENERAL HOSPITAL, NEWCASTLE-ON-TYNE

In this survey of General Medicine most stress is laid upon clinical states arising from war conditions on which fresh work has been done or new opinions have been expressed.

SHOCK

During the year 1940-41 there have been many opportunities for studying the condition of shock. The diagnosis and treatment of shock have been brought into prominence by the war. Despite much work, little more is known of the ultimate causes of this condition than was learnt during the war of 1914-18. It has, however, been confirmed, that reduction of blood volume is one of the most important features of shock, and one that must be promptly treated.

Restoration of blood volume

Recent advances have been concerned chiefly with methods of restoring blood volume. It has been shown that as a transfusion fluid, saline is ineffective and gum saline is unsafe, whereas human blood, plasma, and serum are almost equally effective. Whole blood is preferable if there has been much haemorrhage, but plasma or serum are more useful in the shock of burns. New methods in the preparation and storage of these blood derivatives are now often described. Enthusiasm for the new is unfortunately apt to lead to forgetfulness of the old, and the importance of general measures, such as rest, warmth, and relief of pain, requires emphasis.

Estimation of degree of shock

In estimating the degree of shock it has been shown that the most important single criterion is the blood pressure, especially if serial readings are taken, but reliance must not be placed on this alone as it may be misleading, e.g. in a hypertensive subject. It has been found also that there may be an initial rise of blood pressure at an early stage in the syndrome and if the physician is not aware of this, the mere fact of a so-called normal blood pressure may be misleading. Exactly the same early rise sometimes occurs in the shock associated with coronary thrombosis.

Fat embolism

Fat embolism may produce symptoms suggesting shock, and necropsies have shown fat embolism to be a factor in the death of some air-raid victims, but the relative importance of this condition remains to be established. (See also p. 74.)

Crush injury syndrome

A new syndrome, to be distinguished from shock, has recently been described—the 'crush syndrome'. Persons whose limbs have undergone prolonged crushing may make a good initial recovery, followed later by evidence of renal damage, with oliguria, the passage of pigment casts, and uraemic symptoms, often with a fatal termination. Work on the nature of this syndrome is proceeding and it has been suggested that myohaemoglobin may be formed from damaged muscle and may block the kidneys. (For discussion of Shock see also pp. 8 and 38.)

CARDIOVASCULAR DISEASES

Many problems arise at recruiting boards in the interpretation of both physical signs and symptoms. The significance of murmurs and tachycardia causes the Medical Boards most trouble. The work of the Boards is very thorough, and more sensible decisions are made in these problems than was the case 25 years ago. Tachycardia and raised systolic blood pressure are apt to be

recorded at such examinations and are more often than is realized the result of 'consulting-room nervousness'.

The recruit's heart

More importance should be given to the recruit's peace-time capacity for work and games than to a systolic blood pressure reading of 20 to 30 millimetres above the average normal or to a heart beating unduly fast. The Boards avail themselves of recognized specialist opinion, and doubtful examples of enlargement can be decided by having the heart X-rayed. It is important to refuse for active service those individuals who are obviously potential candidates for the condition known as da Costa's syndrome, neuro-circulatory asthenia, effort syndrome, and disordered action of the heart (D.A.H.). The assessment of the nervous and physical make-up of some recruits enables a doctor with experience of war conditions to prophesy an early breakdown under fire and even in training, and justifies his rejection of the man for the Services. Unfortunately such individuals have been accepted and are already an encumbrance. Some attempt has been made to segregate cases of the 'effort syndrome' for both study and treatment. The conditions of war have not as yet been such as to produce either the numbers or the severity seen in France in 1914-18. Then the breaking point was reached only after months of service in the field. Study of the condition has produced no fact which throws light on its essential causation. From the practical point of view, the important factors are (1) after thorough examination the dogmatic diagnosis of a normal heart; (2) the discovery of other disease; (3) the recognition of the mental state; (4) appropriate retraining, or (5) discharge to a civil occupation of war importance. (See also p. 44.)

Subacute bacterial endocarditis

It is interesting to speculate on the possibilities of occurrence of subacute bacterial endocarditis in the present war, in view of the large number of cases seen towards the end of the war of 1914-18. If the incidence is likely to be as great now as it was then, will opportunities of treatment be afforded which were unknown at that time? Attempts have been made to cure this fatal disease by the use of the sulphonamides, with or without the addition of heparin, but the published cases offer little hope in this direction.

Patent ductus arteriosus

Surgery has come to our aid in ligature of a patent ductus arteriosus. This is a justifiable procedure in the absence of other complicating anomalies; it must be remembered, however, that those with a patent ductus arteriosus may be quite unaffected by this sole anomaly and may enjoy long and useful lives.

Carotid sinus

Interest in the carotid sinus recalls J. Czermak's observations (1866) of bulbous dilatation of a left carotid sinus. Pressure on the sinus may arrest an attack of paroxysmal tachycardia—often if the site of excitation lies in the auricle, and less frequently if it lies in the nodal tissues between auricles and ventricles. Hypersensitivity of the carotid sinus may lead to syncopal attacks, as e.g. in the case of a 'motor-man wearing a high celluloid collar who fainted when he turned his head to the right' (S. Weiss and J. P. Baker, 1933). If a tumour is found in this region it should be removed. Atropine tends to lessen the sensitivity of the sinus.

Hypertension

Renal ischaemia and raised blood pressure

Clinical examples of unilateral ischaemia of a kidney, such as a unilateral atrophic pyelonephritis, have been found to have a definite relation to a raised blood pressure. H. Goldblatt, J. Lynch, R. F. Hanzal, and W. W. Summerville (1933) experimented by placing adjustable silver clamps on renal arteries and so produced hypertension in dogs; there was an increase of both systolic and diastolic pressures and the level of the blood pressure was a measure of the degree of constriction of the renal arteries. A high blood pressure appeared without any other sign of kidney disease and the

kidneys did not lose their power to concentrate urine nor did the urine show albumin or casts. M. Prinzmetal, H. Lewis, and S. Leo (1940) showed that there was no loss of vasomotor control in the vessels since they still responded to dilator and constrictor influences. As a corollary of this work it has been suggested that it is a pressure hydronephrosis which impairs the renal circulation in prostatic enlargement. Cases have also been reported of unilateral kidney disease apparently producing high blood pressure, which has fallen when the offending kidney has been removed; for instance a kidney compressed by growth was associated with high blood pressure and the blood pressure was lowered by the excision of the growth. A similar dramatic fall in blood pressure was recorded on removal of a single tuberculous kidney in a young adult.

Reasons for the phenomenon

To explain the association between renal ischaemia and a raised blood pressure it has been suggested that some pressor substance enters the venous blood from the ischaemic kidney and constricts all the arterioles of the body. It has also been suggested that the pressor substance from the diseased kidney can be neutralized and rendered inert by an anti-substance developed in the normal kidney. Extracts from normal kidneys have been used in an attempt to counteract an experimentally produced hypertension. This is a field for further experimental work and closer clinical investigation.

RESPIRATORY DISEASES

Blast injury

During 1940-41 more instances of blast injury to the chest have been published. The possible effects of direct injury to the chest, of inhalation of dust, and of carbon monoxide poisoning must be recognized and not mistaken for the results of pure blast. Pain in the chest, shallow rapid breathing, cyanosis, and radiological evidence of opacities indicating collections of blood chiefly in the costophrenic angle, and finer general mottling, are the desiderata of diagnosis. As bleeding may be progressive such cases must be managed with care. (See also pp. 10 and 73.)

Influenza

It is probable that many different filter-passing viruses may cause diseases of the respiratory tract which are clinically indistinguishable from one another, just as different types of pneumococci produce the clinical state of pneumonia. It is suggestive also that the severity of virus infection increases as it descends the respiratory tract from nose to lung alveoli. The viruses concerned may also pave the way for invasion by pathogenic bacteria. Since W. Smith, C. H. Andrewes, and P. P. Laidlaw (1933) described their influenzal virus (A), other viruses have been discovered, by T. Francis, Jun. (1940) (influenza virus B), T. P. Magill (1940) (TM virus), J. M. Weir and F. L. Horsfall, Jun. (1940) (virus virulent for mongooses), and R. E. Dyer and I. A. Bengtson (1940) (Q fever virus). Epidemics from year to year may be due to different viruses. Some 'pneumonia-like' diseases resistant to treatment by the sulphonamides may be directly due to a virus infection.

Pneumonia

If 20 new types of pneumococci have been added to 32 types already described, the efficacy of serological treatment becomes very problematical; although there are still those who hold that treatment by sulphonamides is enhanced by the injection of appropriate sera in addition. The discovery of a few pneumococci in the sputum in a case of lung disease does not necessarily mean that the infection is pneumococcal. When types I and II pneumococci are found in a case of pneumonia they are almost always the cause of the lesion. If large numbers of any special type are found they are likely to be responsible; a similar conclusion may be drawn when a specific pneumococcus is found in the blood.

ALIMENTARY DISEASES

Importance of gastroscopy

Although alimentary diseases rank high as causes of loss of work, little new

has recently emerged concerning them. 'Dyspepsia' is a common disease in the army, and a surprisingly high proportion of cases coming under this heading have been shown to be due to organic diseases, chiefly peptic ulceration and gastritis. More use might be made of the gastroscope in the diagnosis of these diseases; certainly its value in the early diagnosis of gastric carcinoma has been well established.

Liver function test

An evaluation of the relative merits of the various liver function tests, including new methods, such as that of the serum choline esterase test, the serum cholesterol esters test, and the intravenous galactose test, is now overdue.

INFECTIVE DISEASES

It is fortunate that in the last two years there has not been any major epidemic; service at home has not produced any new diseases, such as trench fever, which caused so much disability in the war of 1914-18.

Tuberculosis

The anticipated war-time increase in the incidence of tuberculosis is apparently taking place and the frequency of new cases in the Services raises the question whether the existing methods of examination of recruits are adequate; the case for miniature radiography of all recruits is a strong one.

Diphtheria

The campaign for the immunization of all children has the blessing of the Government, but it is doubtful if the desired result can be obtained without some degree of coercion analogous to that used to ensure vaccination. Some doubts have recently been expressed whether the modern methods of preparing diphtheria antitoxin have not robbed it of some of its virtue. It has been said that modern antitoxin, although it contains many more units to the cubic centimetre, is nevertheless relatively ineffective in diphtheria, owing to the fact of the prevalence of the 'gravis' strain of *C. diphtheriae*; yet in the early days of serum treatment striking cures of this form of the disease were obtained. Whatever may be the truth of the matter—and several hypotheses have been put forward—it is salutary that at least our complacency has been disturbed. (See also p. 66.)

Meningococcal septicaemia

This condition is now well recognized by prolonged fever, and pains and skin rashes often simulating erythema nodosum, easily curable by sulphapyridine (M & B 693). (See also p. 58.)

PEDIATRICS

The drug eumydrin (atropine methylnitrate) has acquired a certain popularity in the treatment of pyloric stenosis in infants, but results as yet are by no means conclusive, and a report of 100 consecutive breast-fed infants treated by operation without mortality must be given careful consideration. It must be realized that the use of eumydrin does not represent a new form of treatment, but merely a new adjunct in medical treatment. The mortality in pyloric stenosis is due largely to infection, often acquired in hospital, and the improvement of conditions in hospitals for infants will do more than anything to reduce this mortality. At present, operation is still probably the safest treatment of pyloric stenosis, and the use of eumydrin in general practice is to be deprecated. (See also pp. 13 and 50.)

ENDOCRINOLOGY

Endocrinology remains a field in which great strides are being made, especially by the chemists. It is almost impossible for the average person to keep in touch with the most recent developments; this is especially so on account of the fact that much recent work still requires critical evaluation. In the field of the sex hormones new synthetic analogues are constantly produced; but the problem of diabetes mellitus remains unsolved, and it is quite evident that it is not simply a disease of the pancreas.

Hormone treatment of undescended testis

The hormone treatment of undescended testis has been given extensive trial, and some estimate of its value is now possible. It seems that the majority of undescended testes descend spontaneously if given time, and that in such cases hormone treatment is unnecessary. The cases in which testes do not descend spontaneously are those in which there is some mechanical bar to descent, or a congenital hernia. In such cases operation is necessary, and it appears that pre-operative hormone treatment then substantially increases the success of the operation.

VITAMINS

Those responsible for the production and distribution of food supplies to the nation have made every endeavour to ensure that the necessary amounts of vitamins are supplied. It is quite possible that fewer cases of vitamin deficiency will arise under war conditions (when the essential facts of feeding are kept in view) than in peace-time (when poverty and ignorance lead to a totally inefficient dietary). (See also pp. 49 and 120.)

Vitamin A

In the war of 1914-18 vitamin A deficiency led to night blindness and after that war many cases were seen in the North of England in children.

Vitamin B

The 'beri-beri heart' is now a recognized clinical entity. A rapidly produced generalized oedema, shortness of breath, anaemia, a dilated heart and occasional electrocardiographic changes are the presenting features. The patient is usually found to have been taking a very inefficient diet or to be suffering from alcoholism, and in the type of case under consideration there is no evidence that any other factor is the cause of the heart failure or that the kidneys are involved. The oedema disappears and the heart diminishes in size rapidly after the administration of betaxan, benerva, or other suitable vitamin B₁ preparation. The rapid cure by the administration of B₁ is further proof of the correctness of the diagnosis. Claims have been made that pyridoxin (vitamin B₆) is efficacious in diminishing the rigidity of paralysis agitans. Further observations have thrown doubt upon these claims. (See also pp. 50 and 121.)

Vitamin C

In the poorer districts of large towns, scurvy is not uncommon and the victims are usually bachelors living alone. It has been observed that such patients on admission to hospital improve considerably even before ascorbic acid is administered. Observations on human beings have been made by depriving the subject of vitamin C and it seems to take six months before evidences of scurvy appear. One of the most striking early clinical signs is follicular hyperkeratosis. There is no increase of capillary fragility, this supporting the contention that, though the phenomenon may result from deprivation of hesperidin (vitamin P), it is not related to vitamin C deficiency.

Vitamin D

A single large dose of vitamin D is capable of being stored in an infant and this method may be used as a preventive of rickets.

Vitamin E

Somewhat extensive claims have been made that neuro-muscular diseases, such as the muscular dystrophies, were benefited by the administration of vitamin E. Similar claims have been made in cases of bulbar paralysis, progressive muscular atrophy and amyotrophic lateral sclerosis. When all the published results are considered and in view of the fact that the clinical course of these diseases is naturally very uncertain, this claim is far from being substantiated.

Vitamin K

Further work has confirmed the value of this vitamin or one of its synthetic analogues in the treatment of the haemorrhagic tendency in the new-born, and of obstructive jaundice. There is evidence that administration of vitamin

K to the pregnant mother raises the prothrombin content in the child. (See also pp. 50 and 122.)

THERAPEUTICS

The sulphonamides

Although the efficiency of drugs of this series is proved in streptococcal, pneumococcal, meningococcal, and gonorrhoeal infections, they are used indiscriminately by many. Their true field of usefulness has increased during the last year, and new members of the series have been discovered. By the use of sulphapyridine in large doses and by giving repeated courses of the drug, apparently hopeless cases of abdominal actinomycosis have been cured. (See also pp. 48, 56 and 116.)

Sulphathiazole

Introduced originally for the treatment of staphylococcal infections, sulphathiazole seems to be effective also in bubonic plague. In the treatment of staphylococcal infections, with surgery controlling the primary or secondary foci, 22 recoveries were claimed in 29 cases of bacteraemia, a concentration in the blood of 16–20 milligrams per 100 cubic centimetres being aimed at. (See also p. 116.)

Sulphaguanidine

Of the newer compounds sulphaguanidine seems to be highly effective in bacillary dysentery. It is water soluble, poorly absorbed from the digestive tract, with a resulting high concentration in the bowel and a low concentration in the blood, and therefore of low toxicity and suitable as an intestinal antiseptic. (See also p. 118.)

Sulphadiazine

Sulphadiazine is readily absorbed and remains longer at a high level in the blood; it is eliminated by the kidneys. It diffuses readily into pleural, ascitic, and cerebrospinal fluids. (See also p. 119.)

Toxic phenomena

It has become abundantly evident that the high concentration in the blood necessary to produce therapeutic results by drugs of the sulphonamide series gives rise in some cases to various toxic phenomena such as vomiting, mental depression and other nervous complications, and dermatitis. One of the most serious is the effect on the kidneys. Under certain conditions the acetyl derivatives of the series produce crystals of acetyl-sulphapyridine. These crystals may produce (1) haematuria to be recognized only by the microscope, (2) a gross haematuria, (3) anuria with serious impairment of renal function. Such renal complications seem to have occurred most frequently during the treatment of gonorrhoea. For instance after 12 grammes of sulphapyridine had been administered in one-gramme doses, four-hourly, lumbar pain and haematuria appeared. To counteract this tendency to crystallization it is important to give copious fluids and on the appearance of haematuria to stop the administration of the drug and to flood the system with liquid. (See also p. 116.) (For Chemotherapy in Children, see p. 48.)

Penicillin

Penicillin, the active principle of the mould *Penicillium notatum*, described originally by A. Fleming in 1929, has been the subject of investigation. It possesses a powerful bacteriostatic action against streptococci and staphylococci, and to a less extent against other organisms including *Bacillus anthracis* and *Cl. welchii*, and has little or no toxicity for man. Results of clinical trial are as yet scanty but encouraging, and it seems likely that an important new therapeutic agent has been discovered. (See also p. 120.)

HAEMATOLOGY

Examination of bone marrow

The examination of the bone marrow rather than of the circulating blood would seem the logical way of studying and diagnosing the so-called 'blood diseases', but technical difficulties in obtaining suitable specimens of marrow, and in interpretation of the films obtained have hindered this approach to the subject. The technical difficulties have been largely removed by the intro-

duction of sternal puncture, but the problems of interpretation remain. When diagnosis by ordinary examination of the circulating blood proves difficult, marrow films may easily be obtained by sternal puncture, and if the films are interpreted by an expert, valuable help may be obtained. In the vast majority of cases of anaemia, however, diagnosis can be reached without recourse to this procedure.

Supravital staining of leucocytes

The use of supravital staining of leucocytes is another technical aid to haematological diagnosis, as well as a valuable method of research. Its diagnostic value, however, is chiefly in monocytic leukaemia, so that it is unlikely to be widely used by the ordinary physician. (See also p. 88.)

Haemoglobin

It is evident that our knowledge of the fate of haemoglobin, after the destruction of the red cell containing it, is far from complete, but it has been substantially increased by the work of N. H. Fairley (1940). He has shown that after intravascular haemolysis, the chief circulating pigment is not methaemoglobin but methaemalbumin.

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GENERAL SURGERY

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WAR SURGERY

The surgery of warfare is of necessity absorbing much of the energy and attention of the medical profession. At home the occurrence of casualties in not very great numbers and with considerable intervals has provided a great opportunity for the study of some of the problems involved. The segregation of the injured in special centres, such as those for head cases, chest cases, and plastic surgery is gradually being brought about. Although this plan has obvious advantages for the study of massed groups it must be borne in mind that in warfare, whether the battlefield is abroad or on the home front, multiple injuries are the rule, for high explosives are not selective in their effects.

Rehabilitation

To ensure complete recovery, every one of the injuries requires skilled attention and the main interest from the specialist's point of view may not be the most important aspect of the case when the patient has to face the problem of regaining his place on return to duty or to civil employment. It follows that the early management of casualties is usually the most important step towards recovery, and all surgeons called upon to treat the wounded should be competent to do the best for every kind of injury in the first instance. At a later stage, when the risks of haemorrhage, shock, and infection have been met, some residual problems of a special nature may remain and it is at this stage that special centres will be most useful; but if real progress is to be made in the surgery of warfare most careful observations must be made and recorded.

Records and their value

Complete post-mortem examinations may prove of great value, and although in the study of some of the injuries of the compression type the findings have proved disappointing, nevertheless they should be carried out even when the cause of death appears obvious. The work involved in such examinations and in the keeping of their records is exacting, and can be properly done only at those times when few casualties can be spread out among many medical officers. But it is from the few cases fully studied and accurately recorded that real knowledge is likely to be gained.

The problem of shock

A great deal of work has been done in connexion with the treatment of shock and compression injuries as well as open wounds. No really practical definition, or indeed working conception, of the state of shock is yet available. Whenever the vital processes of the body—circulation, respiration, secretion, and excretion—are seriously disorganized in the early stages of injury, and haemorrhage can be excluded, it is usual to assume that the condition is what is called shock. Phenomena which develop later and are sometimes spoken of as delayed shock are almost certainly of quite a different nature and due to other causes. Some avoid the term 'shock' and speak of the 'reactions to injury', and all admit that it is often impossible to separate the effects of haemorrhage from other possible causes. The phenomena of so-called shock may be due to a number of conditions; minute search has shown that in some cases fat-embolism may play a part and in others active failure of renal function may be the most important factor. In most human beings there is a strong tendency to natural recovery, and how best to assist without embarrassing this natural proclivity remains the problem of treatment.

Treatment

Warmth, fluid by the natural channels, relief of pain, stimulation, and reassurance in alarm and fear, are the first remedies, and the response to these simple but essential measures supplies the indication for either masterly inactivity or blood transfusion. When there are not any signs of recovery or when the latter is delayed there is no single measure or combination of measures equal in efficiency to blood transfusion. In considering the indications for this restorative measure it should be realized that the state of the pulse is an insufficient, and indeed fallacious, guide and that only the instrumental measurement of the blood pressure will suffice. If after a full transfusion there is no resurgence of the vital reserves it is useless to push restorative measures to extreme degrees. But *nil desperandum* must be the motto, for it is wonderful how in the most severe cases the patients have managed to recover and how often old people have survived. The observation of such cases must have heightened the respect of all for the natural resistance of the human body. (See also pp. 1 and 38.)

Indications for operation

In severe shock the standard of recovery which is necessary before some essential operation can be undertaken is difficult to estimate. A natural reaction and a ready response to restorative measures, with a rising systolic blood pressure to over 100 millimetres of mercury, are of good omen, but continuous observation must be maintained, for a sort of late failure is apt to occur. But it is possible to interfere too much with patients extremely ill; fussy attention and 'over the bed discussion' of grave issues must be avoided, and it is well to remember that there are some factors which cannot be measured. There are also dangers in restorative measures, and recently deaths have been recorded from both blood and plasma transfusion. Oedema of the lungs and upset of renal function due to the quantity or the concentration or perhaps the rate of flow of saline infusion may also be insidious factors against recovery. The words of Gerald, that delightful character in *The Cloister and the Hearth*, might usefully be recalled. When speaking of the fate of his soldier companions at the hands of the army leeches he remarked, 'Hundreds have I seen so scratched and pricked out of the world, and tall fellows too, but, lo! if they have the luck to be wounded where no doctor can be had, then they live; this, too, have I seen.'

Compression injuries

The problems arising in compression injuries have proved to be most difficult of solution. It has been found that in those who have been long buried under a weight of fallen masonry, etc. there has supervened a train of symptoms of which the main features are extensive oedema (usually of an extremity with evidence of vasoconstriction) associated with serious general disturbance and diminished urinary output culminating in anuria. Vomiting and thirst occur, the patient is obviously extremely ill and becomes drowsy, comatose, and often dies. The condition, however, is not rapidly fatal and it may continue for some days. No effective treatment has been introduced, but measures usually employed to stimulate renal function have helped, and some patients recover naturally. There is some ground for the hope that, if the oedema can be kept down, the general symptoms will not be so severe. It has been suggested that if the patients are seen before the onset of oedema the latter may be prevented or limited by firm bandaging or by stimulation of the local circulation by means of the Pavex machine. When the oedema and vascular embarrassment are limited to a limb, and when the parts feel tense with a lowered temperature and absence of distal pulse, the conclusion that there is some gross vascular obstruction seems irresistible. In several such cases the vessels have been explored by direct incision; usually there was not any obvious sign of laceration or of local injury to the soft parts, but the vessels were generally constricted over a considerable part of their course. Tension from oedema inside the muscular sheaths was sometimes intense but, when this was relieved by incision, the vessels recovered their normal size and tone. Sometimes there was deep haemorrhage around the vessel or haemorrhage

into its walls. In the latter event arteriectomy at the injured site was followed by dilatation of the vessel below. On other occasions nothing was found to explain the phenomena and no benefit followed even very extensive incisions. Nevertheless, if the condition does not improve, direct incision over the course of the vessel should be carried out, for it may disclose some unexpected lesion and much benefit may result.

Blast injuries

The study of blast injuries is mostly concerned with the changes in the viscera and especially the lungs; these seem to be due to a sudden rupture of the capillaries, leading to haemorrhages and haemorrhagic disruption in the surrounding tissues. Without injury to the parietes, the abdominal viscera may be ruptured or there may be multiple submucous or subperitoneal haemorrhages. In all probability the conditions are somewhat related to caisson disease, with the exception that the changes are very sudden. In some of the cases, both of compression and of blast injuries, abdominal rigidity has been prominent, and the abdomen has sometimes been opened for exploratory purposes, so closely has a ruptured viscus been simulated. Error may be avoided by observing that distension does not appear, that the aspect of the patient is not abdominal, and that neither free fluid nor gas can be demonstrated in the peritoneal cavity while the rigidity gradually diminishes. Familiarity with the condition has brought enlightenment, and the abdomen is not now opened in these cases. Alas, as time goes on and tragedies multiply, new types of injury are met with, as in those dreadful conditions in which those struggling for life in the sea are subjected to the effects of depth charges. Disruption of some solid viscus, or subparietal rupture of the hollow viscera, and especially of the large bowel, has occurred. (See also pp. 3 and 73.)

Management of war wounds

It may now be asserted that the recognition of the principles of a *complete surgical wound toilet*, rest of the injured part by immobilization by some form of retentive apparatus, which is most conveniently applied in the form of plaster of Paris, and infrequent dressings prove of great value in the management of war wounds. Healing is promoted, secondary wound infection rendered less likely, and the discomforts for the patient are much lessened. But encircling plaster should not be used unless the patient can be under skilled supervision for at least four days, that is to say until the risk of any severe infection is past. It is hardly necessary to point out that if infection occurs, the concomitant swelling inside the unyielding plaster may arrest the blood supply, and gangrene may result. The slab technique of plaster application may overcome this difficulty. The outstanding success of the adoption of the principle of rest, carried out with the assistance of plaster, has stimulated experimental workers to inquire into the reasons for this superiority. One of the most fascinating inquiries has been that carried out in connexion with the bearing of movement on absorption from the tissues. J. Trueta and his associate J. M. Barnes (1941) found by careful experimental work that absorption of bacteria takes place only by the lymph stream. When the parts were immobilized in plaster, scarcely any absorption occurred and the effect of injected bacteria as well as of potent poisons, in the form of some snake venoms, was greatly delayed in consequence. The work bears out what has been found clinically, viz. that both the wounded and their wounds generally show very much better progress when rest is considered a major part of the treatment. Rest for the individual undoubtedly plays an important part in the treatment of infection, but rest by immobilization of the affected part seems to have a still greater effect in a favourable direction.

The newer antiseptics

Experimental work has also been carried out on the effect of the newer antiseptics on the living tissues, and it has been shown that chemicals sufficiently powerful to deter, if not to arrest, bacterial activity can be applied to delicate tissue like the brain without affecting its integrity or power of repair. The treatment of wounds by chemotherapy is undergoing extensive clinical trial, and in cases occurring at home it has been possible to compare

those treated by administration by the mouth with those in which the same preparation has been used for local application only. There is not yet enough information to show which of these methods of administration is the more important. But to be of real value, observations carried out in the hope of settling the problem must be accurately made on the nature and condition of the wound, the time which has elapsed before treatment begins, the material used, the exact quantity employed, and the precise method of its application. Then must follow an accurate and detailed record of the result. It is essential that there should be a clear understanding of the purpose of the local use of the new antiseptics. If they can be employed as a first method of treatment to anticipate infection and to destroy bacteria before the latter begin to multiply in the tissues, their value will be enormous. But to have this happy effect it is presumably necessary to distribute the preparation over every part of the wound. With big and complicated injuries this probably means anaesthesia, and it may be that the complete wound toilet can be conveniently carried out at the same time. There is no probability, and certainly no evidence, that a little powder or a tablet or two placed in a wound results in such a diffusion of the antiseptic that sterilization occurs. It cannot be too much emphasized that the surgical toilet of severe wounds involves an operation carried out under anaesthesia and with all the appurtenances required for major surgery. The treatment of the later stages of war wounds is also claiming attention and careful work has already shown that granulating surfaces infected with streptococci can be rendered sterile by dusting with sulphanilamide; no great quantity is required, but just enough to make the surfaces appear as if they had been touched by a severe hoar frost. Antiseptics of the sulphonamide group can be used with confidence, but they are especially effective against streptococci, and as yet there is nothing which would appear to be as nearly specific against other microbes. The preparation of granulating surfaces is especially important in cases in which secondary interventions, such as are necessary in plastic surgery, are contemplated. In these cases the loss of tissue by sloughing may be very detrimental to the success of the procedures and it is therefore essential to determine the state of the wounds bacteriologically before operation. If it is ultimately shown that chemotherapy can be relied upon to bring about the eradication of micro-organisms from wounds, the employment of the sulphonamides and similar drugs will become the most valuable method of preventing recrudescence of infection. This is an important problem in connexion with the subsequent operative interference which is bound to be necessary in a great many cases of war wounds. In the present war sufficient time has now elapsed to produce examples of some of the consequences of war wounds, and the problems associated with non-absorbent foreign bodies are beginning to arise. Nothing in more recent methods of wound treatment has occurred to alter the general rule that sooner or later such foreign bodies are prone to cause trouble. There are also occasional cases of aneurysm, though as yet the type of wound met with does not seem likely to produce that lesion with any frequency; this condition usually develops insidiously and may be discovered by ordinary examination before it produces symptoms likely to command attention. (See also pp. 6, 48 and 115.)

Burns

Burns are still the source of much discussion, and there is as yet no stability about the methods of their management. In civil practice during recent years no improvement has been more striking than that shown by the results of the treatment of burns by the tannic acid coagulative method, and it would be a disaster if this plan were given up because of the peculiar and often tragic circumstances associated with warfare. It may be worth while to restate the general principles which must guide whatever method of treatment is employed. The most effective first-aid measure is to get the patient into hospital as soon as possible; shock must be treated, potential sources of infection must be removed by thorough cleansing usually under anaesthesia, the surface should be so treated as to prevent loss of serum and to limit

absorption, and the general condition of the patient must receive constant attention. Within this general plan all necessary modifications may be made, depending on the stage at which the patient is first seen, the degree of infection present and the part affected. It is probable that the questions involved in the treatment of burns in patients admitted as earlier casualties to hospitals dealing with air-raid victims are quite different from many of those which are incurred in naval warfare, in which immersion in the sea—and often for long periods—adds to the difficulties of the problem. When there has been long delay between the infliction of the burn and treatment, or when there are other associated and serious injuries, or when patients have been long immersed in water, treatment of the casualties is bound to present difficulties and no one method will meet all indications. The region affected adds new factors and this especially applies to the hands, the face, and the neck. Thus the time may have arrived for the exercise of an elective attitude in treatment, but there is no justification for discarding the tannic acid method in its entirety, for it has most certainly stood the test of time in civilian practice. But it cannot be expected that the terrible burns sometimes met with in this war can be treated with success by any one method, and in the presence of such injuries it must be realized that the mortality will be high. Treatment of the more severe burns, such as those of the third and fourth degrees, by excision and early skin-grafting introduces an entirely new principle and its development should be left to those trained in plastic work and with special opportunities for its exercise. (See also p. 113.)

Reparative or restorative surgery

There is a great field for surgical enterprise in connexion with the treatment of deforming and crippling injuries about the face, neck, and hands. But it seems to be a mistake to call this form of surgery plastic surgery, and the description *reparative* or *restorative* specifies the aim of the interference more exactly. The fact that these interventions are so often needed emphasizes the necessity for the most careful and accurate repair of these injuries when they are first sustained. Restorative surgery should be primary surgery whenever possible. One lesson has once again been emphasized in all this war work, viz. the extreme importance of dealing with the whole patient and not only the most obvious or the grossest lesions. It should not have required another war to emphasize this point, which has always been driven home in warfare, but it is well that it should always be borne in mind. In some of the severely wounded, lesser injuries, such as trivial breaches of the surfaces and small foreign bodies, have later been the origin of septic complications which have proved a very serious menace to recovery.

Heparin

In the surgery of the vascular system much is expected from the use of heparin in the prevention of thrombosis and embolism, but there does not seem to be a record of any extensive work with this substance in the United Kingdom. It has, however, been very thoroughly tested by G. Murray (1940) and his associates, and in their hands has proved of great value. In the multiple wounds of warfare there is just the risk that some vessels may not be securely occluded and that the prolongation of the clotting time induced by heparin will interfere with the natural arrest of haemorrhage and thus bring about a serious situation. But with this proviso, it may be said that the substance has proved most valuable in the prevention of thrombosis in operations for arterial suture, vessel grafting, and embolectomy. It is hoped that by means of its use intubation of arteries, to bridge a gap where laceration has occurred, may be carried out without the bugbear of premature thrombosis. Heparin also reduces the symptoms and alleviates local discomforts in thrombophlebitis, and it may be the means of preventing embolism; but it does not lead to the dispersal of clots or thrombi. It is employed by local injection into the vessels at the operative site and by infusion into the blood stream for as long as eight days. It is only the difficulty of obtaining the preparation which has so far limited its use in this country. (See also p. 118.)

CROSS INFECTION

One problem solved may happily initiate another inquiry, and the investigation of the action of sulphanilamide on granulating wounds led to an exhaustive research into the whole question of cross infection in surgical wards. The concourse of many persons—busy nurses, doctors, and visitors—in the wards, the shaking or merely the agitation of bed-clothes, the cleansing of the floors by mops, and dusting generally, all seemed to be factors which might stir up particles and pollute the air. These circumstances are additional to the possible direct conveyance of infection from patient to patient by the dressing of a number of cases in succession. As a result of the investigation the institution of a ward technique eliminating every ascertainable means of infection, and carried out after the ritual of that practised in the operating theatre or even the bacteriological laboratory, resulted in a quite surprising diminution of bacteriologically proved contaminations. Some reform in surgical ward technique is timely, but it is not unfair to mention that those responsible have often fallen away from the teaching of Lister. Older surgeons brought up in that tradition may well feel that the neglect of the protection of antiseptics may be responsible for much cross infection. There will probably come a time when simplification in ward technique will demand consideration, and it is then that the Listerian methods may come into their own again.

NUTRITION AND HEALING

The bearing of the general state of the patient on problems of wound healing has received further study, and the beneficial effects of attention to nutrition and the supplementing of the ordinary dietary by vitamin C, for instance, has received further support. Like the poor, these nutritional problems have always been with us, and patients with 'good healing flesh' and otherwise have always been recognized. It is mainly since the vitamins have been isolated and the means for their recognition established that we have been provided with some measure of the degrees of the sub-nutritional state. Delayed wound healing and disruption of incisions bring the matter urgently before the notice of those in charge. In the management of actual cases not only the type and the quantity of food but its variety and appetizing qualities must be considered. Paré knew a great deal about these matters and his story of the treatment of the case of the Marquis D'Auret with his appreciation of the virtues of the 'great pot' are well worth recalling even though that case occurred as long ago as 1570. (See also p. 113.)

PERITONITIS

In civilian practice the possible use of chemotherapy in intra-peritoneal infections is under investigation. It is hoped, for instance, that local application of one of the sulphonamides may do much to arrest peritonitis and to render residual abscesses less frequent. As yet it is too soon to say what the effect of the use of these substances in the peritoneum may be, and there appears to be a risk that their use may become a routine before their value is established.

CONGENITAL PYLORIC STENOSIS

The subject of congenital pyloric stenosis is again receiving attention and it is suggested that in most cases the drug eumydrin (atropine methylnitrate) is so favourable in its action that operative interference is not likely to be generally required. There seems to be some danger in this connexion of a retrograde step. It must never be forgotten that the operation for pyloric stenosis in infants has proved very satisfactory in the immediate past and the results have been wonderfully good. It would be better if the clinical trial of this new drug could be undertaken in one or two centres at which the results could be most carefully watched and recorded. Until it is possible to make some pronouncement amply supported by clinical evidence it would be unwise to discard what is now the well-tried operation of Rammstedt. (See also pp. 4 and 50.)

MALIGNANT DISEASE

On the treatment of malignant disease much that has appeared supports the

view that when it can be carried out efficiently radical operative treatment usually gives the best result. In this connexion the work of G. Gordon-Taylor (1938) on malignant disease of the breast and of H. Bailey (1941) on parotid tumours are examples of the results that may be obtained. It is indeed a healthy sign that surgeons are again paying close attention to the late after-effects and the bearing which they may have on the nature and extent of operative interference. But the lessons of this evaluation are just as important for those who are working on radiotherapy.

HERNIA

The numbers of communications to the medical press dealing with the modification in the operations for the treatment of hernia show that this matter is not accepted as having reached its final stage. Consideration of the whole subject of hernia suggests that a surgical lifetime might be usefully devoted to the study of the subject in the expectation that some final method might be evolved. Work on this subject emphasizes the need for the greatest care in the preparation of case records and in the continuous following-up of cases. By going through these avenues of rather dull research it is quite likely that some great truths may yet be discovered.

BONE AND JOINT SURGERY

Dislocation of the Intervertebral disks

The association of displacement or dislocation of the intervertebral disks with intractable sciatica seems very definite and there are now many recorded cases in which the most inveterate type of this malady has been completely and permanently relieved by the operative removal of a displaced disk.

Fracture of femur

Operative treatment of *intracapsular fracture* of the neck of the femur with some type of metal pin must now be accepted as the routine for this disabling injury, and when the age of the patient is taken into account the results have certainly been exceptional.

Fracture of olecranon

For many years the treatment of a common injury like fracture of the olecranon was looked upon as standardized, but the principle of the removal of the bone fragments as now practised in treating fracture of the patella is being applied to these injuries. The results are said to be much better than by the other plans which have been accepted as a satisfactory routine for such a long time.

GASTRECTOMY

It is not the purpose of a general review to deal with matters of technique, but it is interesting to note that the original method of gastrectomy by direct union of the divided stomach to the duodenum, as used by Billroth in his first cases, is becoming increasingly popular even among surgeons who for years have extolled operations of the Polya type. The Billroth operation is more nearly a restoration; it is physiological, and ample experience has shown that even after large resections approximation can always be secured, and also that the progress of the case immediately afterwards is almost uniformly satisfactory.

RECTAL SURGERY

In rectal surgery it is also a very healthy sign that efforts are continuously being made to improve on operations for malignant disease and to reduce the mortality of the necessary intervention. The latest plan is to have two operators working simultaneously—one in the abdomen and the other from the perineum. Fortunately there is still a flickering interest in operations in which the sphincteric mechanism is preserved; some of the younger surgeons are tackling the problem. At the Proctological Sub-section of the Surgical Section of the Royal Society of Medicine in 1941 the writer showed six specimens from patients operated upon by the conservative method and who were alive and well or had died without recurrence from 10 to 20 years after operation. Probably there will never be many cases in which this type of

operation can be attempted, but it is a pity to miss the opportunity in the few who are suitable, for the advantages of the preservation of the sphincters are so enormous.

But there are few branches of surgery in which some striking change in practice has not occurred.

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OBSTETRICS AND GYNAECOLOGY

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OBSTETRICS

Posterior pituitary extract in obstetrics

In discussing the dangers and advantages of posterior pituitary extract in obstetrics, J. B. DeLee (1940) states that it may cause shock which, although seldom fatal, is often ominous and may result in permanent after-effects in the brain. As the hormonal balance may be upset, posterior pituitary extract should be avoided in thyroid conditions and in diabetes mellitus. In patients with heart disease it may be used only post-partum, but ergot is better. It is said that in threatened eclampsia it may provoke convulsions. There may be anaphylaxis, with severe urticaria, violent general or local pruritus, oedema of the face, eyes, glottis, or lungs and, in some cases, severe shock. The greatest dangers arise from increase in intensity and duration of the uterine contractions; rupture of the uterus may occur if the resistance to the advance of the child is greater than the strength of these contractions.

Advantages of posterior pituitary preparations

The advantages of posterior pituitary preparations are as follows. (1) *During pregnancy*.—According to DeLee the relaxed ureter in pyelitis can be induced to contract and to expel the stagnant urine. In the case of an abortion in progress after an appendix operation, posterior pituitary may be used for the double purpose of emptying the uterus and overcoming ileus. In septic abortion, after a preliminary course of quinine, 3 grains every hour until five doses have been given, posterior pituitary extract in 5-unit doses given hourly for two hours is helpful in promoting expulsion of retained fragments. (2) *Induction of Labour*.—It is safe to induce labour with posterior pituitary extract but only if proper precautions are observed. DeLee gives half a unit with a tuberculin syringe and, with ether in readiness, watches the effect. At the end of 20 minutes one unit is given and a like dose thereafter every 20 or 30 minutes until an effect is seen. DeLee then stops the injections and, if the force of the contractions dies off, repeats the dose or increases it a little, not using more than 10 units altogether; he has discontinued the use of quinine to sensitize the uterus, as this drug is inefficient and occasionally harmful. (3) *During labour*.—There is no justification for the use of oxytocics during normal labour. For inertia during the second stage great caution is necessary. DeLee is convinced that after complete dilatation of the os uteri, and with the head on the perineum, the application of forceps combined with episiotomy is safer than posterior pituitary extract. In cases of accidental haemorrhage use of the posterior pituitary extract is permissible, with due precautions to hasten labour and to increase uterine tonus, but it is never justified in placenta praevia. (4) *Third stage*.—DeLee discountenances its use as a routine, but it is invaluable in post-partum haemorrhage, although it may occasionally fail. It should be reinforced with ergometrine.

Diabetes mellitus in pregnancy

The discovery of insulin has resulted in an increasing number of women with diabetes mellitus who become pregnant, and within recent years considerable attention has been directed to the dangers to which both mother and child are exposed. Apart from the added risks of coma in badly controlled cases, diabetic women are in a high degree apt to become subjects of the toxæmia of pregnancy. Priscilla White gives an incidence of 21 per cent in 168 cases, E. P. Joslin 45·7 per cent in 35, W. W. Herrick and A. J. B. Tillmann

(1938) 21.4 per cent in 56. The toxæmia is mainly of the hypertensive type, but in a considerable number of cases it is pre-eclamptic and eclamptic. In diabetic women the foetus is liable to be damaged and it is significant that this risk has not appreciably lessened in the insulin era. Thus White records an abortion rate of 22 per cent in the pre-insulin era and 16 per cent in the insulin era, and still-birth rates of respectively 29 and 25; Joslin gives a foetal mortality rate before 1922 of 50 per cent and after that date of 43 per cent. Priscilla White and Hazel Hunt (1940) bring forward evidence that the high foetal death-rate in diabetes mellitus is associated with hormonal disturbances. In a study of 61 patients, they show that (a) when the prolactin was below 200 rat units per 100 cubic centimetres of blood the foetal survival rate was 92 per cent, (b) when the prolactin was above this figure the foetal survival was 42 per cent, (c) the high prolactin figure in abnormal cases is associated with a low oestrogen and a low progesterone level which they regard as the change of primary significance. Among patients treated with large doses of oestrogens, 150,000 to 450,000 international units of oestradiol benzoate and 10–40 milligrams of proluton daily, they obtained a foetal survival rate of 87 per cent. A wide employment of this therapy is financially prohibitive.

Relative incidence of spontaneous and induced abortion

L. C. Rivett (1941) reports an inquiry based upon 2,912 replies to questionnaires received from hospitals in London and the provinces and 344 received from patients treated privately or at clinics. The larger group included 2,402 in-patients and 164 out-patients. The material represents a substantial group of abortion cases of all types, drawn from 17 large towns, three countries and five London County Council hospitals. The forms were for the most part filled in with great care by experienced medical officers who were fully aware of the objects of the enquiry, and there was no reason to doubt the accuracy of the report. In 2,811 cases in which a completed abortion was recorded the results were (1) induced, (a) therapeutic 6, (b) illegal 575, total 581 or 20.67 per cent; (2) spontaneous, (a) known reasons 783, (b) unknown reasons 734, total 1,517 or 53.97 per cent; (3) doubtful, 713 or 25.36 per cent. The sepsis percentage rates were as follows: induced, 14.80; spontaneous, 3.63; doubtful, 3.36. The figures are interesting in that they reveal a high incidence of spontaneous abortions. The finding that the 'doubtful' group has a sepsis rate within the same range as that of the frankly 'spontaneous' cases suggests that it includes a considerable proportion of spontaneous cases.

Habitual abortion

J. S. L. Browne, J. S. Henry, and E. H. Venning (1939) report the result of endocrine assays in 25 cases of threatened and habitual abortion. They give evidence suggesting that in these conditions there may be a disturbance affecting the oestrogens, prolactin, and progesterone. They find that secretion of sodium pregnanediol glucuronide, the secretory product derived from the metabolism of progesterone, tends to rise about the seventieth day from the low level obtained after implantation, but that this rise may be deferred until the hundredth day of pregnancy without untoward symptoms. The authors believe that this rise denotes the stage at which the placenta takes over from the ovary the secretion of progesterone and that the secretion of this material throughout pregnancy depends upon an adequate output of prolactin. They find evidence that progesterone formation, as estimated from the amount of pregnanediol excretion, is diminished in cases of abortion. Henry, in an analysis of 500 cases of abortion, found that the onset of symptoms took place on the average at the eighty-first day, i.e. at about the time of the transition between the ovarian and placental phases. Accordingly they believe that in habitual abortion progesterone therapy should be concentrated during this period. The minimum dose should be 5 milligrams given daily or every other day and increased if bleeding occurs. R. E. Campbell and E. L. Sevringhaus (1940) used progesterone in the treatment of 13 pregnant women, of whom 12 had had two or more abortions without living issue and one, although she had had one successful pregnancy, terminating in the birth of a mature living baby, nevertheless had two abortions in subsequent pregnancies.

Of these, eleven went to term and gave birth to living children without abnormalities. C. G. Collins, J. C. Weed, and J. H. Collins (1940) believe that wheat-germ oil combined with progesterone and, when necessary, thyroid extract, is of value in the treatment of threatened and habitual abortion. In discussing the place of vitamin E in the treatment of habitual abortion the American Council on Pharmacy and Chemistry state that the clinical evidence is still unconvincing but that the published reports are sufficiently encouraging to justify further clinical experiment, provided that steps are taken to ensure that only preparations of vitamin E of known activity are used. The synthetic product *dl*- α -tocopherol acetate, recently put on the market as ephynal, seems to have solved this difficulty.

New classification of toxæmias of pregnancy

The American Committee on Maternal Health propose a new classification in an endeavour to obtain a simple and uniform formula in place of the many unsatisfactory and often chaotic classifications at present in existence. They suggest (1) hypertensive disease, (2) renal disease, (3) pre-eclampsia (severe) and pre-eclampsia (mild), (4) eclampsia, (5) vomiting of pregnancy, (6) acute yellow atrophy of the liver, and (7) unclassified.

Pre-eclampsia and eclampsia and renin

R. J. Kellar and J. K. Sutherland (1941) discuss recent experimental work on hypertension and its possible bearing on the late toxæmias of pregnancy. It is some years since Herrick and Tillmann first showed that a woman who becomes hypertensive during pregnancy runs a 50 per cent risk of persistent hypertension in after-life. G. W. Pickering (1936) and M. Prinzmetal and C. W. Wilson (1936) showed independently that in so-called simple hypertension, in malignant hypertension, and in nephritic hypertension, the basic fault was a hypertensivity of the small vessels which was not nervous and was therefore presumably chemical in origin. Pickering and Prinzmetal (1938) then repeated the long-forgotten work of R. Tigerstedt and P. G. Bergman and confirmed the fact that in the rabbit's kidney there is a relatively powerful pressor substance, renin. Kellar and Sutherland investigated the cases of 35 pregnant women with hypertension and 22 normal pregnant women, and concluded that the hypertension of pregnancy was similar to essential hypertension in being probably chemical and not nervous in origin. In experiments on rabbits and rats, Kellar and Sutherland failed to discover any increase in sensitivity to renin in the pregnant as compared with the non-pregnant animal. Weight for weight, the kidney of the pregnant doe did not appear to contain more renin than that of the non-pregnant doe. These observers found no renin-like pressor substance in the placenta of the rabbit or of the rat. Further, neither the normal nor the toxæmic human placenta, when tested on the rabbit or rat, was found to contain any renin-like pressor substance.

Pregnanediol excretion during pregnancy

C. L. Cope (1940) studied the pregnanediol excretion in 100 cases of pregnancy, of which 75 were pathological. The substance was extracted from the urine in the form of sodium pregnanediol glucuronide and was weighed. During the luteal phase of the menstrual cycle the total output per day varies from 3 to 60 milligrams, the maximal excretion occurring 5–7 days before menstruation. During the early weeks of pregnancy the excretion does not exceed that of the peak in the menstrual cycle. The maximal output occurs in the last two months of pregnancy. Pregnanediol cannot be demonstrated in the urine a few days after delivery. During the last 6 weeks of pregnancy the daily excretion varies from 30 to 110 milligrams, the average being 55 milligrams. There are wide variations within normal limits, and the absence of pregnanediol does not exclude pregnancy. In abortion a negative pregnanediol test on at least two occasions usually means that abortion is complete or that the products of pregnancy are dead. Chronic nephritis and toxæmia of pregnancy interfere with pregnanediol excretion, so that negative results are sometimes obtained. Nevertheless, in 10 cases of toxæmia the output of pregnanediol was within normal limits.

Georgeanna Seeger and Eleanor Delfs (1940) record a case in which a continuous series of pregnanediol determinations were made throughout pregnancy, both ovaries being completely removed on the 63rd day. The pregnancy continued normally to term although the pregnanediol excretion remained throughout far below that usual in pregnancy. On only two occasions did it slightly exceed the values present in non-pregnant menstruating women. The prolactin and oestrogen values were similar to those obtained in normal pregnancy.

Effect of bombing on labour

R. C. Brown (1941) reports 4 cases in which he believes that the emotional distress caused by the severe bombing of London between August and October 1940 caused a curious change in the character of labour. In these patients, three of whom were primigravidae, the os was dilated and the cervix taken up and thinned out at the first examination and the patients were regarded as in labour, although labour pains were absent. Nevertheless at subsequent examinations the cervix was found to be dilating progressively as the result of what Brown regards as a greatly prolonged and painless first stage. In three of the patients these phenomena were discovered a considerable time before actual delivery (38, 18, and 12 days respectively) and in the fourth they were discovered 5 days before. In each case the second stage was extremely short, varying from 1½ to 3 hours in the 4 cases. Brown states that members of the nursing staff of the City of London Maternity Hospital had seen during the period of bombing many women who were delivered after a labour (presumably restricted to the second stage) lasting only 2 to 3 hours.

Pyelitis of pregnancy

W. T. McConnell and L. A. Gray (1940) studied the urinary tract in 12 normal primigravidae by intravenous pyelography before and after delivery. The subjects were all between the ages of 17 and 22 years. Before delivery 9 showed hydronephrosis on the right side and 3 on the left. In 10 cases re-examination was made in the period of 10 days after delivery, and 2 of these which had shown moderately large hydronephroses before delivery had returned to normal, 2 were unchanged, 2 had a slight reduction in the dilatation, but in 2 there was a definite increase. Three cases with marked dilatation showed no evidence of a return to normal even at the end of 7 to 14 weeks. In 28 patients who had had pyelitis of pregnancy 5 months to 14 years previously (17 right side, 8 bilateral, 3 left side) McConnell and Gray found a right hydronephrosis in 20 (71 per cent), left hydronephrosis in 15 (53 per cent), and hydro-ureter on the left side in 10 (35 per cent). In 2 patients stones were present in the left kidney. In only 2 cases were the pyelograms normal.

C. M. McLane (1939) reports 168 cases of pyelitis out of a total of 14,000 deliveries, 106 antenatal, 62 postnatal. The cases occurred nearly equally in primigravidae and multigravidae. Only 12 gave a former history of pyelitis. No intimate relationship between toxæmia and pyelitis was recognized. The incidence of recurrence was 5 in 168. McLane emphasizes the importance of a regular review of cases at monthly intervals until 3 cultures are negative. A subsequent pregnancy is discouraged until the cultures are negative for 2 years, and when the first attack is severe McLane advises treatment in the period between pregnancies and during subsequent pregnancies. He reports that 3 out of 10 cases occurring before the 16th week were so severe that therapeutic abortion was required. Of the 98 antenatal cases 46 had a febrile postnatal course. With persisting positive cultures the disease should be regarded as chronic and apt to produce progressive fibrosis of the ureter and renal pelvis. The author believes that the infection is derived from the bladder along the lymphatics of the ureter. The maternal mortality in his series was 3.58 per cent and the foetal mortality 15.8 per cent.

Induction of labour by uroselectan B

P. L. Playfair (1941) reports on the use of uroselectan B for the induction of labour in 115 cases. The bladder is emptied, and after the presence of intestine in front of the uterus is excluded, the presentation and back of the foetus are determined. The skin between the umbilicus and symphysis pubis is prepared

and at a point midway between these two landmarks the structures of the abdominal wall down to the peritoneum are anaesthetized with 2 per cent novocain solution. A medium-sized lumbar puncture needle with a stillette is pushed through the skin, anterior abdominal wall, and uterine wall, the needle being directed away from the back and head of the child. Usually the membranes are felt on the end of the needle, which is then gently pushed through the membranes and the stillette withdrawn; liquor amnii then escapes. If undue resistance indicates that the needle is impinging on the foetus, it is withdrawn from the uterus and pushed through in a different direction and further from the foetal back. In no case is uroselectan injected unless liquor amnii is first obtained; failure to obtain liquor amnii occurred once only in the series. Uroselectan B, 10 cubic centimetres, is then slowly injected, the stillette replaced, the needle withdrawn, and a collodion dressing applied. The patient rests for one hour and then is able to get up and, if an out-patient, to return home. The method is contraindicated if there has been previous operation and sepsis, with possible adhesions of bowel to the abdominal wall. Out of the 115 cases 74 were primigravidae and 41 multiparae. If labour pains did not occur within 76 hours, the case was regarded as a failure; this occurred in 4 cases. The success rate was thus 96.25 per cent, about the same as that with artificial rupture of the membranes and far better than that obtained with pituitary derivatives during a similar period. There were 86 normal deliveries, 14 by forceps, 2 by Caesarean section (both after failure), 1 assisted breech case, and 1 shoulder presentation with a dead foetus, ending in decapitation. The maturity of the cases varied between 22 and 44 weeks. The average time for the induction was fairly constant between the 36th and 44th weeks (27 to 29 hours), with a tendency for the interval to be less at the earlier weeks. The corrected foetal mortality was 3.6 per cent.

Relief of labour pains by raspberry leaves

J. H. Burn and R. E. Withell (1941) published the result of an experimental investigation of the action of extracts of raspberry leaves on the uterine muscle. Raspberry-leaf tea has been a herbalists' remedy for many years and is said to be the best known and oldest of all the herb infusions and to be included 'as a proved aid in maternity in the most ancient of herbal books'. The statement made to the authors by one firm of herb specialists was as follows: 'Raspberry leaves are the dried leaves of *Rubus idoeus* (*Rosaceae*), which grow in Europe, Canada, and northern United States. The leaves impart their properties to water, giving to the infusion an odour and flavour somewhat similar to that of some kinds of black tea. Raspberry leaves have astringent properties, and they also act as a stimulant. It is found that if the infusion be taken freely before and during confinement, parturition is easy and speedy.' Burn and Withell tested dried raspberry leaves on the uterus of animals, and found that they contain a principle readily extracted with water, this principle relaxing the smooth muscle of the uterus and the intestine when the latter is in tonic contraction. The action is exerted in the body of the cat and also when excised uterine muscle is suspended in a water bath. The relaxation produced in the body increases with successive doses. The same principle, or a somewhat similar one, causes contraction of the uterus of the rabbit in situ, and also of the isolated uterus of the cat, the rabbit, and the guinea-pig when these are not in tone. B. Whitehouse (1941) records his clinical experience of the extract in three women in the puerperium which seems to confirm, so far as the human puerperal uterus is concerned, the observations made by Burn and Withell. The main effect is relaxation of the uterine muscle. The contractions are diminished in force and frequency, secondary contractions are eliminated, and any contractions which may occur are evenly spaced. Raspberry-leaf extract was used in labour cases with apparent relief of pain. It has been suggested that it might be of value in painful menstruation.

GYNAECOLOGY

Insufflation of the tubes

I. C. Rubin (1940) first devised tubal insufflation with oxygen in 1919 as a

method for determining tubal patency in sterility. Carbon dioxide was later substituted for oxygen, because the latter was apt to cause persistent shoulder pain. Carbon dioxide has the advantage that it is more soluble, more rapidly absorbed, and less apt to cause embolism. The additional use of the kymograph in 1925 made it possible to record the graph of insufflation, and thus to recognize normal and abnormal contractions in the tubes, the former being rhythmic and regular, the latter as found in pathological tubes being irregular and atypical. During a 20 years' experience Rubin in 5,269 insufflations found complete tubal obstruction in 32.4 per cent and partial obstruction in 33.1 per cent.

Sterility

S. R. Meaker and S. N. Vose (1940), from their investigation of childless marriages extending over 13 years, conclude that in 90 per cent evidence of infertility can be shown to exist on both male and female sides. In 100 cases, the female was entirely at fault in 14, the male in 8, and in 78 the responsibility was divided, being chiefly on the female side in 15. In male infertility the chief cause is depression of the spermatogenic function due to constitutional factors, endocrine defects, chronic intoxications, and poor hygiene in regard to diet and exercise.

Irritable bladder due to cervicitis

In 1930 J. Young showed that treatment of chronic cervicitis was often followed by the relief of associated urinary symptoms, frequency and dysuria. He also showed that in the majority of such cases there was no evidence of disease in the urinary tract, and that the symptoms were probably due to a local reflex sympathetic disturbance of the bladder mechanism. Such women, in addition to the complaint of cervical leucorrhoea, often mention dyspareunia and iliac fossa pain. J. P. Greenhill (1940) recorded similar findings after treatment of the chronically infected cervix by the electric cautery, ionization, electro-coagulation, or Sturmdorf's trachelorrhaphy. These methods should not be employed just before or after menstruation or in the presence of acute or subacute genital infection.

Intermenstrual pain

E. F. McLaughlin (1940) records 57 cases with ovarian disturbance causing this symptom. Among 23 ruptured cysts there were 10 of follicular type, 11 luteal, 1 follicular and luteal, and 1 undetermined. In 22 cysts with intracystic bleeding there were 16 luteal, 4 of undetermined type, 1 follicular, and 1 follicular and luteal. The average age was 25.8 years. The chief confusion in diagnosis was in respect of appendicitis. It was the primary diagnosis in 36.8 per cent of all cases and in 44.4 per cent of the cases in which operation was performed. The right ovary was involved in 64.5 per cent of the cases.

Oestrogens in uterine bleeding

K. J. Karnaky (1940) believes that both normal menstrual bleeding and dysfunctional bleeding are determined by an oestrogenic bleeding level in the blood. At this level the spiral arteries of the endometrium become constricted, leading to ischaemic necrosis and then to bleeding. The author claims good results in irregular and excessive uterine bleeding with stilboestrol by mouth (10–25 milligrams) or oestradiol benzoate (20,000 to 50,000 rat units) intramuscularly followed by 5 milligrams of stilboestrol every night by mouth for 20 nights, or by 10,000 rat units of oestradiol benzoate intramuscularly every other day until 6 to 10 injections have been given. The author believes that fibromyoma seldom causes uterine bleeding. The latter is usually due to hormonal influences, because it can be controlled in 98 per cent of cases by oestrogens.

Testosterone propionate in excessive and irregular uterine bleeding

W. C. Sturgis, A. R. Abarbanel, and D. S. Nader (1940) state that testosterone leads to a diminution of blood-flow in the uterus owing to its action on the myometrium. It inhibits rhythmic contractility. The average minimal dosage required to lessen the bleeding materially varies from 10 to 30 milligrams. In their series they found that the dosage required to stop the bleeding was 10

to 120 milligrams (average 40 to 60 milligrams). Two to four injections at intervals of 2 to 4 days were usually sufficient. The subcutaneous route gives the most effective 'per dose' action, but when the bleeding is profuse the intramuscular route gives a more rapid action.

Associated pulmonary and uterine tuberculosis

J. E. Lackner, W. Schiller, and A. S. Tulskey (1940) found endometrial tuberculosis in 2 out of 134 biopsy specimens (1.60 per cent) in 125 women with active pulmonary tuberculosis.

Effect of combined administration of prolan and the pituitary synergist on the human ovary

C. Mazer and E. Ravetz (1941) point out that human pregnancy urine yields a luteinizing principle derived from the placenta (prolan). In the ovaries of most species it produces all the effects of the pituitary gonadotrophins. It is, however, incapable of stimulating to any appreciable degree the ovarian follicles of hypophysectomized animals, intact monkeys, and human beings. It is therefore assumed that the pituitary bodies of animals other than the monkey and the human being contribute, in some unknown manner, to the ovarian response to chorionic gonadotrophin. The authors, with a commercial product (synapoidin) containing prolan and the pituitary synergist, have evoked one or more menstrual flows in 19 out of 23 severely amenorrhoeic women, some of whom had not menstruated for years, despite all other forms of treatment. Only 2 have thus far menstruated without further treatment. The injection of the combined extracts arrested dysfunctional bleeding in 14 out of 18 girls, 4 of whom were suffering from puberty haemorrhage. The increased effectiveness of prolan with the addition of a pituitary extract containing very little of the gonad-stimulating hormones is variously explained as follows: (1) that it represents merely the expression of a combined physiological activity, (2) that chorionic gonadotrophin converts a pro-hormone in the pituitary extract into an active gonad-stimulating hormone, (3) that most anterior pituitary extracts contain a principle capable of converting prolan into a universal gonad-stimulating substance.

Effect of large dosage of prolan

W. E. Brown, J. T. Bradbury, and Ida Metzger (1941) administered 500 rat units of antuitrin S for 4 to 6 weeks to 12 patients with a normal menstrual rhythm; 7 did not show any significant change in rhythm, but in 5 there was induced amenorrhoea lasting from 1 to 5 months. This amenorrhoea was accompanied by a progressive atrophy of the endometrium, indicating a suppression of ovarian function. These results indicate that prolan is gonadotoxic or gonado-inhibitory when given in sufficient dosage.

Sterilization in puerperium

Between July 1935 and June 1940 W. N. Thornton and T. J. Williams (1941) performed 309 sterilizations in the puerperium. The operation has been carried out at intervals varying from a few hours to 21 days post partum; it should be performed as early in the puerperium as is feasible. It should be avoided in infected or potentially infected cases. Spinal anaesthesia was used in 297 cases, general anaesthesia in 9, and local anaesthesia in 3. In 219 the Pomeroy technique was employed, in 86 a modified Kehrner operation, and in 3 the Madlener technique. There was one death, that of a patient with diabetes mellitus in whom pyelitis, pneumonia, and severe acidosis occurred. The authors state that 'it was an error to have sterilized her, as the diabetes mellitus was poorly controlled, and her general condition was unsatisfactory'. Of the patients, 226, or 73 per cent, have been kept under supervision and no subsequent pregnancies have occurred.

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ALIMENTARY TRACT DISEASES

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GIARDIA INTESTINALIS

Infection of the small intestines with *Giardia* (or *Lamblia*) *intestinalis* is an occasional cause in Great Britain of recurrent attacks of diarrhoea with or without abdominal pain, and generally among those who have lived in the tropics or subtropics, but sometimes among those who have never been abroad. As a specific cure has recently been discovered, it is very desirable that the symptoms and treatment of giardiasis should become more widely recognized.

Protozoology

Giardia is a flagellate protozoon which inhabits the duodenum and jejunum and leads to catarrhal enteritis without ulceration. It occasionally gains access to the gall-bladder by way of the bile ducts, and it may then give rise to chronic cholecystitis. In the tropics giardia cysts are often found in the formed stools of healthy people, although much less often than the active flagellate in the stools of patients with diarrhoea or dysentery. In acute attacks of dysentery it is associated with *Entamoeba histolytica* or *Bacterium dysenteriae*, but it may persist when such infections have died out, in which event it is probably the cause of the intermittent attacks of diarrhoea, which may continue for long periods even after the patient has returned to a temperate climate.

Clinical picture

In Great Britain *giardia* may give rise to recurrent attacks of diarrhoea with abdominal distension and discomfort, which is occasionally accompanied by the passage of large quantities of mucus containing enormous numbers of the active flagellate protozoa. In such patients the diarrhoea is almost certainly the result of *giardia* enteritis. At the Mayo Clinic F. A. Kyser and H. R. Hartman (1941) analysed the records of 100 patients whose stools were found to contain *giardia*. In 60 there was diarrhoea, in 65 abdominal pain, in 10 vomiting, and in 6 fever. Irritability, general weakness, and other nervous symptoms were present in 34; these symptoms appeared to be a result of the infection, because improvement or complete recovery followed elimination of the giardial infection. In 11 the organism was found incidentally without any symptoms which could be attributed to its presence. These figures correspond closely with the relative frequency of the symptoms of giardiasis as it occurs in Great Britain.

Infection of gall-bladder

Giardial infection of the gall-bladder may give rise to cholecystitis. I have seen one such case in a patient who had never been out of England. In this case and in several described by B. B. V. Lyon (1936) the bile obtained through a duodenal tube after injection of magnesium sulphate contained enormous numbers of active *giardia*. In several cases the bile from a chronically inflamed gall-bladder immediately after operation showed many *giardia* (P. de Muro, 1939), and a similar finding has been made at necropsy.

Treatment

Many drugs have been tried for *giardia* but until recently none had proved to be effective. In 1939 B. Galli-Valerio discovered that atabrin (mepacrine, atabrin) acted as a specific in eradicating the infection, and his observations have since been confirmed by Muro (1939), L. M. Morrison and W. A. Swalm (1939), and Kyser and Hartman. One 0.1 gramme tablet is given three times a day after meals for 5 days. This always results in the permanent disappearance of the organism from both the stools and the bile.

DIVERTICULITIS AND COLO-VESICAL FISTULA

The investigations of W. H. M. Telling in 1908 and 1920 demonstrated that colo-vesical fistula is generally a result of diverticulitis and not, as had previously been believed, of carcinoma of the pelvic colon. On theoretical grounds it was assumed that the correct treatment of such a fistula was to perform a colostomy at once and, if possible, to separate the colon from the bladder at a later date. The most recent papers on diverticulitis repeat this teaching, in spite of the fact that H. C. Edwards in 1937 brought forward conclusive evidence, founded on an experience of nineteen cases, in favour of more conservative treatment. He showed that colostomy does not always result in closure of the fistula, and in one case a fistula actually developed after a colostomy had been performed for obstruction. A subsequent operation for separation of the colon from the bladder is always extremely difficult, and in one out of four cases in which it was performed the fistula recurred.

Effect of faeces in bladder

The bladder is remarkably tolerant of the presence of faeces. Consequently bladder symptoms are rarely severe, except sometimes during the first few months after the development of a fistula. In nearly every case of colo-vesical fistula attacks of diverticulitis are less frequent and less severe after its development than before, the fistula apparently acting as an efficient safety-valve. The colon bacilli and enterococci in normal stools are not pathogenic. Moreover, formed faeces contain comparatively little soluble material, none of which is of an irritant character. Consequently the introduction of small quantities of faeces into the bladder through a fistula does not necessarily cause cystitis on account of either its bacterial or chemical constituents. The actual perforation is a result of inflammation, but when the acute attack of diverticulitis which preceded perforation has subsided, cystoscopy generally shows that the inflammation is confined to the immediate neighbourhood of the fistula, the rest of the bladder wall being unaffected by the contamination of the urine with faeces. In only one of Edwards's nineteen cases was there any evidence of ascending infection—a single attack of pyelitis, from which the patient recovered. Attacks of subacute cystitis are likely to complicate each recurrence of acute or subacute diverticulitis, and also to occur with diarrhoea even in the absence of diverticulitis, since unformed and liquid faeces swarm with bacteria and contain large quantities of the toxic products of bacterial activity.

Management of the case

A patient with diverticulosis and a colo-vesical fistula is thus often very little the worse for it, and generally much prefers the minor discomfort which he may have from time to time to the perpetual inconvenience of a colostomy. It is of great importance that his stools should be kept formed but soft; diarrhoea is much more dangerous than constipation, because soft or fluid faeces easily escape through the fistula, whereas solid faeces pass it by. The patient should never take aperients; paraffin, which is very useful in uncomplicated diverticulitis, makes the faeces too sticky and too apt to enter the bladder. The right consistence of the stool is obtained by giving just enough of a vegetable mucilage, such as isogel, which contains no phenolphthalein or other purgative, the presence of which makes most proprietary mucilages unsuitable. On such a régime little or no faeces may enter the bladder for long periods, although small quantities of gas may escape from time to time, often at long intervals, without causing any pain. The fistula is in fact valvular and generally remains closed for long periods. If an attack of cystitis develops, rest in bed and the administration of sulphathiazole for forty-eight hours are generally sufficient to overcome it. The patient should take a full diet, but should avoid pips and skins of fruit, raw vegetables, and other 'roughage'. With these precautions attacks of diverticulitis are unlikely to occur. The presence of even slight pain in the left iliac fossa or difficulty in getting the bowels open is an indication for the administration of belladonna to overcome the spasm which is likely to be present. The dose, which

varies greatly in different individuals, should be the maximum the patient can take without having toxic symptoms.

PATHOGENESIS OF THE SPRUE SYNDROME

The sprue syndrome

T. E. H. Thaysen (1932, 1935) has given good reasons for regarding sprue, non-tropical sprue, and coeliac disease as varieties of the same disease. Coeliac disease differs from sprue only in showing characteristics which depend upon its occurrence in young and growing children. There is not any difference between coeliac disease as it occurs in European children whether it develops in the tropics (when it is likely to be called sprue) or in Europe, or between tropical and so-called non-tropical sprue. As Thaysen pointed out, the tendency to regard diseases which are more common in the tropics as differing fundamentally from similar conditions occurring in non-tropical countries is quite unjustifiable. True beri-beri occurs in England and even in Iceland and Newfoundland as well as in hot climates whenever the essential dietetic deficiency is present, and the same is true about pellagra, which was long regarded as a purely tropical disorder. Thaysen gave the name *idiopathic steatorrhoea* to the group of diseases comprising sprue, non-tropical sprue, and coeliac disease. But this does not give any indication that the steatorrhoea consists in the excretion of split fat in the form of fatty acids and soaps and not as neutral fat.

T. I. Bennett and C. Hardwick (1940) grouped together coeliac disease, tropical sprue, non-tropical sprue, and the various rare conditions which give rise to a similar clinical syndrome under the heading of *chronic jejuno-ileal insufficiency*. It is useful to have a name which indicates that the symptoms are a result of functional insufficiency of the small intestine, and that a similar picture is produced by any condition which interferes sufficiently with the normal physiological activity of the small intestine. But the term chronic jejuno-ileal insufficiency does not properly emphasize the specific nature of the insufficiency, namely, the inability of the small intestine to absorb split fat. This deficiency is constantly present in all the conditions under consideration even in their mildest form, so that in their absence the sprue syndrome can be excluded absolutely. On the other hand, intestinal carbohydrate dyspepsia is also a form of jejuno-ileal insufficiency, but is entirely independent of the sprue syndrome, with which it is never associated. The *sprue syndrome* seems to be the best designation for this group of disorders. (A. F. Hurst, 1942).

Stools in the sprue syndrome

The only constant abnormality in the stools of sprue, non-tropical sprue, and coeliac disease is the presence of excess of unsplit fat in the form of fatty acids and soaps and the absence of excess of neutral fat. This can always be recognized by microscopical examination of the stools, which renders the much more laborious estimations of neutral fat, fatty acids, and soap superfluous. There are generally no other abnormal constituents; there are no striated muscle fibres, such as are found together with excess of neutral fat in cases of pancreatic insufficiency, and there is no increase in the nitrogen excreted in the faeces. Bennett and Hardwick refer to the intestinal carbohydrate dyspepsia of the sprue group of disorders, but F. A. Knott found that there was not any excess of undigested starch granules in a single one of our cases at New Lodge Clinic, whereas the presence of starch granules without excess of meat fibres or of fat in any form is characteristic of intestinal carbohydrate dyspepsia. The stools, moreover, produce none of the excess of odourless gas on incubation, which always develops in intestinal carbohydrate dyspepsia (A. F. Hurst and F. A. Knott, 1931).

Mechanics of fat absorption

The lipase of the pancreatic juice splits neutral fat into fatty acid and glycerol. Bile salts combine with the fatty acid to form water-soluble complexes, which are absorbed by the epithelial cells lining the villi of the small

intestine. The fatty acid is set free and combines with glycerol within the cell to form neutral fat, which passes into the central lacteals of the villi. The contents of the central lacteals are pumped into the larger lymphatics by the rhythmical contractions of the villi caused by the activity of the muscularis mucosae, extensions of which pass from the main layer in the submucosa to the apex of each villus.

The valvulae conniventes

The normal feathery or herring-bone appearance of the duodenum and jejunum, which is the radiographic manifestation of the valvulae conniventes, disappears in the sprue syndrome. The opaque material separates into smooth outlined masses of various lengths. With clinical recovery the normal appearance of the small intestine returns. This radiographic sign is constantly present. It has been described especially by D. K. Miller and W. H. Barker (1937) (in connexion with sprue), A. M. Snell and J. D. Camp (1934), J. L. Kantor (1939) and R. Golden (1941) (in non-tropical sprue), and R. Golden (1941) (in coeliac disease). G. Forssell (1923) proved that the pattern of the normal valvulae conniventes seen with the X-rays is constantly altering owing to the activity of the muscular mucosae.

Morbid anatomy of the sprue syndrome

Most of the changes formerly described as occurring in the intestines in sprue have been shown to develop *post mortem*, as they can be prevented by the injection of formalin into the abdominal cavity immediately after death. The slight inflammatory changes occasionally found and the still less common ulceration are the result of secondary infection or, more probably, as Thaysen has suggested, of long-continued irritation by fatty acids and soaps.

Thaysen (1932) performed a necropsy on a missionary, aged 48, who died from sprue contracted in China six years before. Immediately after death 2,000 cubic centimetres of 10 per cent solution of formalin were injected into the abdominal cavity. No macroscopic or microscopic changes were found in the mucosa or submucosa of the intestines; there was not any desquamation, degeneration, or atrophy of the epithelium of the villi or of Lieberkühn's crypts, and no increase in plasma or connective tissue cells in the submucosa. In two cases examined by F. P. Mackie and N. H. Fairley (1934) immediately after death and while the intestine still showed peristaltic movements, no atrophy or inflammatory lesion of any part of the alimentary tract was discovered on naked eye and microscopical examination.

A similar absence of pathological changes in the intestine was observed (a) by Thaysen (1932) in a fatal case of non-tropical sprue, in which post-mortem changes were prevented by the injection of formalin into the abdominal cavity immediately after death, and (b) in a biopsy made during an exploratory laparotomy on a man with non-tropical sprue, in whom during life Golden (1941) had demonstrated the characteristic radiographic changes of the small intestine.

Paralysis of the muscularis mucosae and the sprue syndrome

Paralysis of the main layer of the muscularis mucosae results in flattening or disappearance of the valvulae conniventes and the disappearance of the characteristic changes in the mucous membrane pattern of the duodenum and jejunum observed in the sprue syndrome. If there were paralysis of the extension of the muscularis mucosae into the villi there would be a cessation of the pumping action of the villi; consequently fat would cease to be absorbed, but the activity of the pancreas would be unaffected so that the digestion of fat would take place as usual. The stools would consequently contain a great excess of split fat but no excess of neutral fat, i.e. they would have the characteristic features of the stools of sprue and coeliac disease. Such paralysis would not alter the microscopical appearance of the mucous membrane, and restoration of normal fat absorption with reappearance of the valvulae conniventes would follow recovery of the functional activity of the muscularis mucosae.

The cause of the functional failure of the muscularis mucosae, if this is in truth the cause of the sprue syndrome, remains a mystery. It might be due to

absence of the unknown constituent of the chyme which is the chemical stimulant of Meissner's plexus (the nerve centre of the muscularis mucosae), or to the effect of vitamin deficiency or to some specific or non-specific toxæmia on the plexus or, less probably, on the muscularis mucosae itself.

Lacteal obstruction and the sprue syndrome

If the above explanation is correct, the cases presenting identical symptoms, which result from lacteal obstruction by disease of the mesenteric glands and to which J. A. Ryle (1924) has specially drawn attention, differ from the more usual cases of the sprue syndrome only in the hindrance to fat absorption being situated at the mediastinal gland level instead of in the villi. Obstruction of the lacteals by tuberculous glands, and less frequently by glands affected with Hodgkin's disease, lymphosarcoma and secondary carcinoma is the cause of the majority of cases of non-tropical sprue, together with a small number of typical cases of sprue occurring in the tropics (I. D. Jones, 1924) and of coeliac disease. The distinction can be made only if a laparotomy for some independent condition such as acute appendicitis is called for (as in Ryle's cases and in the two recorded by Jones), in rare cases in which the X-rays show the presence of calcified mesenteric gland, and at necropsy. In a case of this kind under the care of Professor L. J. Witts, in which a large mass of calcified mesenteric glands was found on X-ray examination of the abdomen, the jejunum showed the normal feathery appearance with the X-rays in contrast to the smooth contour found in clinically identical cases without organic obstruction of the lacteals.

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AVIATION MEDICINE

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Under modern high-speed and high-altitude flying conditions, it is important that aviators should be alert in body and mind, with accurate vision, good muscle tone, quick reaction-time, and a good sense of balance. The standard clinical examination, as used in the Royal Air Force, to help in the assessment of physical fitness for air crew duties has been dealt with in detail by T. S. Rippon, in Vol. II of this *Encyclopaedia*. The results of such tests, however, do not predict the individual's aptitude to learn to fly. Thus, H. L. Burton, E. C. Chambers, and A. F. Rook (1939) followed up the flying training to the end of a year of a batch of 106 sub-standard candidates as judged by the existing clinical tests and a control batch of 103 candidates who had passed as up to standard. The sub-standard group consisted mainly of men with cardiovascular instability and hypotension of a degree considered correctable by Service training. The proportion of failures to learn to fly was practically the same in both groups, namely, 20.75 per cent in the sub-standard and 19.4 per cent in the control group; but none failed to learn to fly for any medical reason rendered apparent by the clinical efficiency tests. These clinical tests were designed, however, to assess general physical fitness to withstand years of stress of flying at home and abroad under both peace and war conditions, and it is believed that they are useful for this purpose and that they form a basis on which to give judgement on normal health and to assess the possibilities of any future alteration in the physiological state.

In this review two aspects of aviation medicine are dealt with: (1) pre-selection for flying duties; (2) maintenance of the physiological efficiency of flying men.

PRE-SELECTION OF MEN FOR FLYING DUTIES

About 90 per cent of those who fail to learn to fly at all, or within the average time, do so because of inherent lack of flying ability, this being mainly due either to poor power of muscle-joint coordination and to a slow reflex reaction or to some psychological factor; the latter would appear to account for the major proportion of failures to learn to fly.

Flying aptitude

On the assumption that those with deft hands and feet will handle the controls of aircraft more adroitly than those who are ham-handed and lead-footed, a so-called 'Flying Aptitude Test' has been devised by G. O. Williams (1939), in which his arm-leg coordination or sensori-motor apparatus is used. This apparatus tests fine and graduated coordinated movements of one arm and both legs, while the person under examination is distracted from time to time by visual and auditory signals, and has to respond thereto with the other arm in a manner somewhat similar to that of the coordinated movements performed by an aviator piloting an aeroplane. Williams's researches have shown that the application of these sensori-motor tests to candidates on entry eliminate about one-third of the potential failures to learn to fly among those who are physically fit.

Williams's apparatus

The apparatus used by Williams consists of a pilot's seat and adjustable rudder bar and control column with its movement limited fore and aft, together with a suitably illuminated and geared test cabinet, mounted at eye level two feet in front of the pilot's seat. This cabinet is fitted with a circular domed screen of opalescent glass, 10 inches in diameter. Cross lines mark the centre of this screen, and a $1\frac{1}{4}$ -inch square is marked centrally on the cross.

A spot of light, activated by a disk which revolves inside the cabinet, moves in a definite but irregular course across the screen for a period of 100 seconds. The candidate has to neutralize the irregular movements of this spot of light and keep it central on the screen by means of the rudder bar for lateral, and the control column for vertical, deviations. Distractions, such as a red and white light in front of the cabinet and a buzzer, have to be counteracted as quickly as possible by moving a lever with the left hand in the appropriate direction. A system of differential gearing records the score on four separate disks for leg movements, arm movements, reaction to distractions, and total score respectively. This test gives a numerical record of the candidate's ham-handedness or lead-footedness.

Cardiovascular stability

In the selection of fighter pilots who are so liable to be exposed to sudden variations of acceleration, it is of the utmost importance that they should have good cardiovascular stability. As pointed out by Rook (1939), persistent hypotensives should not be accepted for aerobatics. Failure of the diastolic pressure to rise efficiently on change from the horizontal to the vertical position indicates instability for high-speed flying. According to C. L. Leedham (1940) 20 per cent of the cream of the American youth applying for acceptance for flying training in the United States Army have to be rejected on account of vasomotor instability; this is an incidence much higher than that of the United Kingdom.

Fitness for high-altitude flying

When flying in ordinary types of aircraft at a height above 30,000 feet and even at low rates of ascent, man is liable to suffer from decompression sickness or 'bends', the condition being akin to caisson disease in deep-sea divers. The common symptoms in order of frequency are itching of the skin, joint pains which may be incapacitating, visual disturbances, localized oedema of the skin, and, if exposure is continued further, paralysis, pulmonary oedema, and unconsciousness. The symptoms do not appear immediately on reaching 30,000–37,000 feet, but are developed often after an hour or more; they disappear when the aviator comes down to about 25,000 feet, except that blind spots, sick headaches, and haziness may remain for some hours. It is considered that these symptoms are due to the nitrogen dissolved in the body fluids coming out of solution more rapidly than it can be disposed of by the lungs, thus forming gas bubbles in the blood vessels and in certain tissues, particularly those of a fatty nature, which helps to explain the symptoms and also the fact that obese individuals are more prone to suffer from 'bends' than those of a spare build. B. H. C. Matthews, T. C. Macdonald, and J. C. Gilson (1939, 1940, 1941), as a result of extensive experiments carried out in the low-pressure chamber, have demonstrated that it is possible to produce decompression sickness and 'bends' in about 50 per cent of apparently normal individuals, when the latter are submitted to rapid rates of climb to altitudes of 30,000–37,000 feet in from $\frac{1}{2}$ to $1\frac{1}{2}$ hours, the exact period of time varying with the individual, his physical condition and habits. Only about 25 per cent of fit spare-built individuals suffer from 'bends' when submitted to the standard selection test in the low-pressure chamber. It is thus possible to make a pre-selection of individuals for particular duties as regards their height tolerance. H. G. Armstrong and J. W. Heim (1940) claim that the inhalation of pure oxygen for $\frac{1}{2}$ –1 hour before ascent, and while muscular exercise is carried out, prevents the onset of 'bends' by elimination of much of the nitrogen from the body; but it is more correct to say that pre-oxygenation delays the onset of 'bends'.

Night visual capacity

For night flying, it is important to select those who have not only good light-and-dark adaptation, but who possess also good form sense. To test for night visual capacity a number of different techniques have been devised. E. E. Metcalfe (1940) uses a colorimetric test, based on the fact that the normal eye after exposure to glaring light returns to normal gradually as regards colour sense, green being the last colour to return. C. E. Ferree and

G. Rand (1939) use an electrical multiple-exposure tachistoscope, a somewhat complicated instrument which, in addition to testing dark adaptation power, measures the speed of adjustment of the eyes for change of distance and speed of accommodation, testing also for ocular fatigue. In the Royal Air Force, however, P. C. Livingston's (1932) Light Sense Apparatus was used to assess the night visual capacity of flying men but, as this apparatus tested only one individual at a time, Livingston (1940) devised a new apparatus, called the *Rotating Hexagon*, which is capable of testing six persons at one sitting. The apparatus consists of a revolving hexagonal drum, each face being similar and having a series of illuminated panels showing letters, figures, and forms, such as ships, arrows, crosses, and similar devices. Thirty-two different forms and objects can be presented under varying illuminations, the whole apparatus being readily portable. The method in vogue is that of passive adaptation; the subjects wear, for half an hour in an ordinary lighted room, special dark goggles fitted with filters which have a light transmission of 3.36 per cent, followed by fifteen minutes' further adaptation in a fully darkened room. Then the dimly illuminated letters, figures, and silhouettes in the rotating hexagon are exposed for reading. The full score obtainable is 32, and the results are classified as follows:—

Exceptional	—	—	30 to 32 marks
Above average	—	—	26 „ 29 „
Average	—	—	13 „ 25 „
Below average	—	—	5 „ 12 „
Poor	—	—	0 „ 4 „

The night visual capacity of 6,000 fit males, of the age group 18 to 30, tested in this manner was as follows:—

Exceptional	—	—	4.8 per cent
Above average	—	—	15.2 „
Average	—	—	61.1 „
Below average	—	—	16.3 „
Poor	—	—	2.6 „

Stereoscopic vision in relation to landing of aircraft

There are two valuable tests in use in the United Kingdom to assess stereoscopic vision at various optical planes and so to help to assess the individual's judgement in approach and landing of aircraft. These tests are made by use of (1) the *Angular Depth Perception Apparatus* and (2) the *Rotating Stereogram*.

(1) The Angular Depth Perception Apparatus of Livingston (1939) is a three-pin test which permits rotation of the pins in parallel through a complete circle for the purpose of removing binocular vision when judging distance; it is most difficult to assess the relative position of the pins as regards distance when binocular vision is not in operation, i.e. when the pins are horizontally placed. In addition, the pins are made of fine wire (1 millimetre in diameter) to overcome, as far as possible, the factor of size of objects in the analysis of distance. Results are recorded graphically while the middle pin is moved by the individual under test as he endeavours to judge its position relative to the two fixed outer pins.

(2) The Rotating Stereogram was devised by Livingston (1939) to ascertain the visual conception of depth and whether or not stimuli are reaching consciousness through both eyes simultaneously (important factors in preparing to land aircraft). The stereoscopic sense can be estimated by this apparatus as a percentage of normality. The apparatus is used with the Holmes stereoscope and consists of a special holder for a pair of stereoscopic pictures which can be rotated through 180° by means of a centrally placed cog-wheel; this permits of an infinite variation in the stereoscopic values of the pictures. There are 10 pairs of pictures, which are translucent and so may be used with the amblyoscope in the orthoptic treatment of ocular muscle imbalances. Such orthoptic training has proved most successful in improving the landing performances of pilots, or of would-be pilots, suffering from certain forms of ocular muscle imbalance.

Psychological pre-selection of flying personnel

Extensive investigations have been carried out during the past two years, not only in the United Kingdom but also in Canada and the United States, to devise suitable tests for the psychological pre-selection of flying personnel based on the characteristics considered necessary in the temperamental make-up of the various members of air-crew—pilot, observer, air-gunner—as well as their aptitude for bomber or fighter duties. This matter is still *sub judice*.

MAINTENANCE OF THE PHYSIOLOGICAL EFFICIENCY OF FLYING MEN

In the advancement of aviation, the man is as important as his machine, a fact apt to be forgotten in this mechanical age. As far as is practicable, the machine must fit the man instead of the man fitting the machine, and to ensure this, design of aircraft and flying equipment should be carried out in conjunction with physiologists and certain other medical scientists. The high speed, range of flight, and complexity of modern aircraft, together with the need for operating at ever higher levels, which enable the aircraft to develop more speed at less power than at lower levels, to avoid stormy weather and bumpy air, and to attain protection from enemy anti-aircraft fire, have led to a great increase in stress and strain on the human element, demanding a high degree of physical fitness of air-crews and constant supervision of their physiological requirements. Among the problems to be solved are oxygen want (including parachute descents from high altitude), blacking-out, cold, mental and physical fatigue, noise, vibration, glare, and air-sickness.

Oxygen want or anoxia

In the fit individual, so far as aviation is concerned, symptoms of oxygen want or so-called 'altitude sickness', such as dulling of the judgement and intellect, unwarranted sense of well-being and security, delayed reaction time, tachycardia, dyspnoea, and muscle weakness, do not usually occur until a height of 15,000 feet has been reached and maintained for about half an hour, the period of time and degree of affection varying greatly with different individuals. The symptoms occur much more quickly if moderate exercise, such as moving about in the aircraft, is indulged in. Heights above 25,000 feet cannot be long attained without the use of oxygen, since otherwise unconsciousness and death would quickly occur, owing to decrease in the total and partial pressure of the oxygen in the air, with consequent low percentage of oxygen in the blood and tissues. As a result of oxygen want, the depth of breathing is markedly increased, so that at 20,000 feet, without additional oxygen, each inspiration may comprise a volume of from 1,000 to 1,200 cubic centimetres of air. The rate of respiration, however, changes little with altitude. Death from altitude sickness in the normal individual is probably always due to failure of the respiratory centre. The exposure period (without additional oxygen) required to produce death is progressively shortened with altitude. Thus, at 25,000 feet, death is liable to occur within half an hour.

The ill-effects of oxygen want are first noticeable at 10,000 feet if that height is maintained for an hour or so, mental alertness being diminished and sleepiness tending to occur. At heights above 15,000 feet, without additional oxygen, visual acuity and light sense are decreased, and at 18,000 feet auditory acuity becomes rapidly diminished, so that at 20,000 feet the aircraft engine noise may be imperceptible. Convincing and early signs of oxygen want are deterioration of handwriting and inability to do simple arithmetic. The degree of change in man's mental and physical output is directly proportionate to altitude and length of exposure. The earliest symptoms of oxygen want are comparable and similar to those of alcoholism: the individual loses the power of self-criticism and consequently is oblivious of the fact that he is suffering from oxygen want. Strict orders are therefore laid down regarding the heights at which additional oxygen must be taken. Among the means taken to prevent oxygen want in present-day aviation are training of men in the low-pressure chamber and the development of improved

types of oxygen apparatus, so that an adequate supply of oxygen may be ensured at all times, and in all atmospheric conditions, with the minimum of waste. The after-effects of anoxia are headache and fatigue, which may persist for many hours; these may increase in intensity and duration in proportion to altitude, so that in addition there may be nausea, vomiting, dizziness, mental confusion, muscular weakness, and prostration.

Parachute descents

It has been shown by experiments in the low-pressure chamber that, if the oxygen supply were to fail suddenly and completely at 35,000 feet, a drop would have to be made to 20,000 feet within $1\frac{1}{2}$ minutes to prevent onset of unconsciousness, even if the individual concerned were sitting quietly; muscular work, such as movement, would use up more oxygen, and so shorten this safety period or 'interval of reserve'.

The rates of parachute descents have been computed from known physical facts, as well as from actual observations made during descents, mainly by von Diringshofen (1939) and by H. Armstrong (1939) and his co-workers in the United States of America. The rate of descent of man with open parachute varies directly with his weight and inversely with the density of the atmosphere, as indicated in tabular form below. On baling out at 35,000 feet, the rate of free fall varies according to the speed of the aircraft, and rapidly becomes about 160 feet per second or 110 miles per hour, but this is reduced, by the opening of the parachute, to about 36 feet per second or 25 miles per hour at these heights.

Approximate Rate of Descent of a Man, weighing 10-11 Stones,
with Open Parachute 25 Feet in Diameter

HEIGHT (IN FT.)	RATE OF FALL (IN FT. PER MIN.)
35,000	2160
30,000	1980
25,000	1800
20,000	1620
15,000	1500
Ground level	1200

Thus, if an aviator escaped from an aeroplane at 35,000 feet, and opened his parachute rapidly, he would take about 10 minutes to reach 20,000 feet, by which time he would probably have died of anoxia. In fact, unconsciousness is apt to occur within 3 minutes, and death within 10 minutes at the height of 30,000 feet, if a person is suddenly deprived of his oxygen supply. It will be realized that a valuable part of the reserve time interval referred to above is spent in getting out of the aircraft, and that the more severe the muscular exertion in this process, the shorter will be the reserve time. A parachutist could reach the safety zone by doing a free fall from 35,000 to 20,000 feet in $1\frac{1}{2}$ minutes before opening his parachute, but there is the danger of his becoming too anoxaemic to remember to pull the rip-cord in time. To help ensure a physiologically safe descent a light portable oxygen set has been devised by W. M. Boothby, O. O. Benson, Jun., and W. R. Lovelace, Jun. (1940).

Blacking-out

Blacking-out first became a problem of importance in aviation during the period of training for the Schneider Trophy races in 1929, when aeroplanes had developed sufficient speed to produce centrifugal forces greater than 5 'g' while performing sharp turns or being pulled out from steep dives at high speed. The term 5 'g' here implies a pressure of 5 times the body weight, which in the normal sitting posture is exerted through the long axis of the body. The sharper the turn, provided the speed is kept constant, the greater is the centrifugal force and the greater is its effect on the human body. Thus, an aircraft travelling at 300 miles per hour, if turning on a 500-yard radius, is subjected to 4 'g'; at 420 miles per hour on the same radius the 'g' attained is nearly 8.

The onset of blacking-out is sudden, but it does not occur immediately an excess over 5 'g' is applied, when the pilot or passenger is in the normal sitting position; there is a period of delay lasting a variable number of seconds, depending on such factors as the amount of 'g' applied, the general physical and vasomotor tone of the person concerned, and the anticipation of or preparedness for the manoeuvre performed; in the average pilot, blacking-out does not occur until 4 seconds have elapsed after a force of 5 'g' is applied and held.

Blacking-out is due to centrifugal force acting in the long axis of the body from head to feet and so causing most of the blood to flow rapidly in that direction, leading to pooling of the blood in the abdomen and legs; this was shown by U. Fischer (1937) in monkeys, by means of X-rays mounted on a centrifuge. The brain and heart are thus drained of much blood; the blood pressure falls considerably (S. Ruff, 1938; Matthews, W. K. Stewart, and G. E. Watt, 1940, 1941). Such lowering of the blood pressure reduces the pressure in the central artery in the retina, which is normally about half that of the brachial artery, to such a degree that the balance between intra-ocular and vascular pressure is upset, and as a consequence the circulation of the blood in the central artery of the retina is stopped, thus causing blacking-out of vision until the balance is readjusted by a return of the blood pressure when the centrifugal force falls below 5 'g'. At forces of less than 4 'g' (as shown by R. Koenen and O. F. Ranke, 1937), the action of the carotid sinus reflex is sufficient to prevent the blood pressure from falling low enough to cause blacking-out.

The main symptoms of high 'g' in a healthy man are, first a feeling of the tissues of the face and eyes being sucked inwards and downwards, then of the abdominal contents being displaced downwards; this is quickly followed by a gradually increasing dimness of the whole visual field; then sudden blindness or blacking-out occurs, and at the same time there is frequently a tingling sensation in the calves of the legs. Records taken by Matthews, Stewart, and Watt with the cine-camera in the aircraft at the time of blacking-out, however, have shown that even fit individuals may suffer momentarily from impairment of consciousness. The blacking-out period lasts a varying length of time, usually about 2 to 5 seconds, depending on the force and duration of the 'g' applied; it passes off as suddenly as it occurs while the loop or turn is being completed at a force less than 5 'g'. There may be a certain lack of mental concentration for a few hours after a blacking-out, and some individuals suffer from headache and insomnia on the same night, but in the trained and fit pilot, blacking-out does not occur so readily as in the unfit, and after-effects are usually not evident.

The great danger of blacking-out is the momentary loss of complete control of the machine by the pilot during a critical manoeuvre, such as trying to get on the tail of his adversary, with the result that the former is thus apt to be placed at a disadvantage; while, to prevent blacking-out occurring during aerial combat, the pilot may avoid high 'g' turns and so by his slowness of manoeuvre fall a prey to a quicker and more venturesome enemy. It is important therefore that a pilot should be able to obtain the utmost manoeuvrability of his aircraft compatible with avoidance of blacking-out or strain of the structure of the machine. Researches undertaken to find means of the prevention of blacking-out, in Germany by von Diringshofen (1936) and in this country by Matthews, Stewart, and Watt, have proved that if the pilot adopts a crouched sitting position with legs raised during high acceleration, he can withstand without blacking-out about 2 'g' more than in the normal sitting posture. An additional aid is to yell loudly during a manoeuvre likely to cause blacking-out and thus raise the diaphragm and further increase the intra-abdominal pressure. At the same time all flying personnel should keep fit, should practise exercises to increase the tone of the abdominal muscles, and should be abstemious as regards alcohol and tobacco. They should not, if possible, do aerobatics until an hour after a meal, as a loaded stomach reduces resistance to blacking-out.

Various types of belt have been tried to give increased support to the

abdominal wall and so to lessen the gravitation of blood to the lower parts of the body during high acceleration. Certain people have from time to time recommended the use of belts to prevent blacking-out, on the assumption that the chief cause of this phenomenon is the pooling of blood in the abdomen. Experiments show that this is not the case, as most of the blood gravitates to the legs. Experiments with plain belts, air-filled belts, and water-filled belts have proved that, at any rate in their present form, they are entirely unsuited for the use of pilots as a preventive of blacking-out. Some of the belts raise the blacking-out threshold by about 0.7 'g', but, when this point is exceeded, the wearer not only blacks-out but becomes unconscious, as the belt interferes with the proper return of blood to the heart, as the 'g' is passing off.

There are, however, various other circumstances which lower man's resistance to 'g', such as oxygen lack in the tissues due to deficient intake at altitudes; carbon monoxide intoxication from exhaust fumes; alcohol or tobacco intoxications, even of the previous day; and the after-effects of certain illnesses.

Protection against cold

The temperature of the air decreases on an average 1° C. for each 500 feet ascent until the height of 36,000 feet is reached; above that altitude, the air temperature remains constant at -55° C. throughout the year. In aircraft the cold may be greatly lessened by warmth from the sun, or it may be intensified by draughts. Severe cold leads to arteriolar spasm and pain, followed by local death and insensitivity of the tissues involved—this is termed 'frost-bite'; the hands, feet, nose, and ears are the parts affected first. Continued exposure to cold causes a lowering of the body temperature, and slowing of circulation and respiration, accompanied by anoxia leading to physical and mental sluggishness and profound sleepiness. Oxygen deficiency or want during high-altitude flying, therefore, aggravates the ill-effects of cold and must be carefully guarded against.

The most satisfactory method of protection against cold in aircraft is by efficient cabin heating off the exhaust or by special boilers; when this is not practicable, recourse must be made to retention of body heat by the wearing of suitable flying clothing or by providing additional heat through electrically heated gloves, boots, and clothing. It is of the utmost importance to ensure that no tight-fitting clothing is worn, and particularly gloves and boots, otherwise the circulation is impeded. All clothing must be dry, to prevent undue heat loss from the skin. Hot drinks and carbohydrates should be taken frequently and muscular movements of the limbs indulged in as often as possible to increase heat production and stimulate the blood flow. For treatment of frost-bite see the *Encyclopaedia*, Vol. V, p. 440.

Fatigue

There are various factors at work in causing fatigue in aviation, such as the stress of taking off with heavily laden machines or landing at high speed; the mental anxiety of night flying or flying through fog; the discomfort of a confined and cramped position; loss of vitality due to cold; the effect of noise on the auditory nerve; and anoxia when the oxygen supply is inadequate.

Preventive measures to combat these fatigue-producing factors include robot pilots, improved wireless apparatus, and direction finders to simplify night and blind flying; the proper design of seats to avoid cramping; air-conditioning of cabins and the provision of suitable and easily donned flying clothing to maintain agreeable temperature in all climates and at different heights; sound-proofing of cockpits and cabins and the wearing of specially designed flying helmets (as described in the next paragraph) to minimize aeroplane noise; and, last but not least, the provision of an adequate oxygen supply, the necessity for which must be impressed upon all, especially the captain of the aircraft and the crew. Those engaged regularly on flying duties require adequate relaxation and rest, particularly sound sleep, otherwise mental and nervous energy are proportionately decreased, and, if the loss of sleep is continued, there will be a gradual but definite fall in efficiency, as the

batteries of life run down in a manner somewhat similar to the effect of a short in the circuit of an electric battery.

The effect of aircraft noise on auditory acuity

Noise in aircraft is derived mainly from the engine, from revolutions of the crankshaft and propeller, and from aerodynamic turbulence; propeller-tip noise is the greatest, is most marked in the plane of the propellers, and is radiated in closed machines from walls, floor, and roof, but not in equal degree; noise in any sector of the cabin is least in the centre and greatest at the walls. The effect of noise on man depends on its level in the sound scale. Sounds between 80 and 90 decibels are disturbing, the degree depending on individual sensitivity, whereas sounds above 90 decibels are deafening, the more so as the scale is ascended, and at or about 120 decibels they produce the feeling of pain. Continued exposure of the unprotected ear to sounds above 80 decibels leads eventually to various degrees of nerve deafness. In the non-sound-proofed cabin there is noise between 90 to 100 decibels in intensity. As a result of sound-insulation of walls and the use of good sound-absorbing inner lining, noise has been so decreased that conversation in a modern commercial aircraft is as easy as in a train. In Service aircraft it is not practicable to reduce the noise by sound-proofing the fuselage, owing to weight. Instead, flying helmets with earphones are used, so designed as to reduce aircraft noise to the minimum while giving good intercommunication reception.

E. D. D. Dickson, A. W. G. Ewing, and T. S. Littler (1939) have demonstrated the loss of auditory acuity resulting from prolonged and repeated exposure of the unprotected ears of pilots to present-day aircraft noise with intensities of 110 to 135 decibels; there is cochlear degeneration with loss of sensitivity to high tones as evidenced by a fall in the hearing in the region of 4,096 cycles per second. The affliction is apt to occur after a hundred hours' flying with unprotected ears, and is temporary at first; it becomes permanent later, the degree varying with individuals. It is an interesting point that although the predominant note in propeller-tip and engine noise is at the lower end of the hearing scale (between 100 to 200 cycles per second), the loss of hearing is always in the higher level of the scale (in the region of 4,096 cycles per second). Protection of the ears with the standard Service flying helmet with earphones appears to prevent this auditory deterioration (Dickson and Ewing, 1941).

Visual problems

Two important visual problems are protection against glare and night vision.

(1) *Glare* is especially apt to affect the eyes of aviators when engaged in flying over clouds, desert, or water, also when flying towards the sun. To overcome this, specially designed goggles are used; these are provided with triplex glass filters of various tints, appropriate for day or night flying, or with polaroid lenses, which are interchangeable and can be slipped in quickly while flying. There is also a dark vizor which can be tilted into position in front of the goggles to enable the pilot to fly, or the gunner to aim, if necessary, directly towards the sun, with the minimum of glare effect. In addition, such goggles help to protect the eyes against fire, missiles, dust, and draughts.

(2) *Night vision*.—For night vision it is necessary, in the first place, to pre-select those who possess good visual acuity and dark adaptation power, as well as good form sense, so as to be able to recognize objects quickly in the dark, as described above. Important adjuncts to improve night vision are pre-adaptation by wearing special dark goggles, an adequate intake of vitamin A and, according to C. P. Stewart (1941), vitamin C; and the use of oxygen at night at heights above 7,000 feet, as proved by R. A. McFarland and J. N. Evans (1939).

Air-sickness

This is akin to travel-sickness (see the *Encyclopaedia*, Vol. XII, p. 222). The incidence of air-sickness varies with the type of aircraft and position of the aviator in the aircraft, being most common in the tail position. There are

a number of factors which have been shown to predispose to air-sickness—cold, discomfort, noise, vibration, smells, diet, and fatigue.

Precautionary measures include sound rest the night before a flight, to increase resistance to fatigue; evacuation of bowels before a flight; a good meal eaten slowly about an hour before taking off; avoidance of fats; small meals consisting of hot tea or coffee, and carbohydrates taken about every four hours during long flights; the wearing of warm clothing and the avoidance of discomfort from cramped sitting positions; the protection of the ears against aeroplane noise by means of ear-plugs or the flying helmet, as this noise leads to fatigue and so predisposes to air-sickness; the occupation of the mind during flight is a most effective means of avoiding air-sickness. Drugs to prevent air-sickness should be given under medical supervision only. The commoner ones used are chlorotone, atropine, or one of the barbiturates; to be effective, these require to be taken about half an hour before the intended flight and may require to be repeated during long flights.

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BLOOD TRANSFUSION IN RELATION TO TREATMENT OF SHOCK

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At the end of two and a half years of war involving the urgent treatment of many thousands of air-raid and military casualties, blood and plasma transfusions may be said to have become firmly established as invaluable resuscitation methods. But as the *Lancet* pointed out in a review of the lessons learnt during the first severe air raids, blood transfusion is not a panacea for all the traumatic states hitherto classified as 'shock'. Indeed future researches will probably be centred on the problem of improved differentiation of a number of clinical conditions which have up to the present been very loosely described, and which together comprise this unstable syndrome. More accurate diagnosis will then become possible; also a clear indication of the occasions on which transfusion is essential.

MODERN OPINIONS ON SHOCK

In order to summarize the progress already made, it may be best briefly to review the development, since the commencement of hostilities, of prevailing opinions on shock. It was once customary to describe two forms—primary and secondary—the first occurring soon after injury and being in the nature of a prolonged faint of vaso-vagal origin, the second developing later and representing a state of true collapse.

Primary shock

The first and obviously milder condition is accompanied by slowing of the pulse and some pallor and sweating. The vagal stimulation causes vasodilatation, fall of blood pressure, and allows the blood to collect in the splanchnic area. It should tend to pass off spontaneously and should be readily amenable to treatment by rest, warmth, and sedatives.

Secondary shock

The second and much more serious state, although also showing pallor, sweating, and a low blood pressure, due in this type to a reduction of blood volume by loss of plasma through the walls of the blood vessels, may be associated with cyanosis, a low body temperature, rapid, rather shallow breathing, and a pulse which usually tends to be small and rapid. In this severe type loss of plasma must result, unless haemorrhage as well as injury has occurred, in a rise in both the haemoglobin percentage and the red cell count. After haemorrhage has taken place dilution of the blood by withdrawal of fluid from the tissues should tend to neutralize the above increases. If the blood loss were sufficiently severe, both the percentage of haemoglobin and the red cell count might actually fall. Certainly if the patients were the subject of haemorrhage alone, both figures must sink below the normal levels. In short, severe shock concentrates, and haemorrhage dilutes, the blood; the blood count must vary according to the condition which predominates. In either event, whether the question is one of raising blood volume or of making good the loss of blood, it has been held that appropriate transfusion of plasma or whole blood could be relied upon to meet the deficiencies. On the above definition, whole blood would be needed only when there had been haemorrhage, and for shocked cases without haemorrhage, plasma transfusions should suffice. At the outbreak and in the very early days of the present war,

this apparently simple distinction dominated much of the practical resuscitation work.

Memorandum on wound shock

The Medical Research Council's *War Memorandum No. 1* on wound shock published in 1940 soon brought to the notice of all a number of possible exceptions to the rule. It was emphasized that even when facilities for immediate transfusion were available, the prompt treatment of fatigue, cold, pain, and restlessness, the prevention—despite the fact that haemorrhage may have ceased—of plasma loss from severely injured areas, and the administration of oxygen might be all important. Transfusion of blood or plasma was awarded only the position of the most valuable single method of combating shock, and its essential mechanism was described as restoring effective blood volume and increasing oxygen carrying power; the quicker the blood volume was restored, the better the prognosis. The *Memorandum* went on to state that when the reduction in blood volume was so great that arterial pressure was significantly decreased, transfusion of a single pint would obviously be insufficient; thus administration of several bottles was advised. Moreover, since symptoms of shock may readily reappear, particularly after the recurrence of haemorrhage, the setting-up and maintenance of drip transfusions during or after operation was advocated. With regard to the substance to be used in transfusion, the value of whole blood was held to be proved whether the symptoms arose from general loss of blood or from local loss of plasma; but it was wisely pointed out that the average case required a much larger amount than had usually been given. Human plasma and serum, since they keep so much better and longer, were considered as important as whole blood, because in some cases reduction of blood volume is due entirely to plasma loss, and even in haemorrhage it may be just as, or possibly more, important to raise the blood volume, serum proteins, and blood pressure as to increase the oxygen carrying capacity. In any case, plasma and serum were held to be superior to solutions such as saline and gum saline, use of which is not without risk. The dehydration, from which all shocked and wounded patients may be assumed to suffer, was to be combated by copious simple drinks containing about half a teaspoonful of common salt to the pint.

Most observers will agree that the advice as given in the above summary and the relative assessment of anti-shock measures have to a large extent stood the test of some eighteen months' practice. The *Memorandum* certainly made clear all the basic circulatory changes which might occur in 'shocked' patients. Unfortunately the vital question still remained how most rapidly and certainly to decide what was happening in each individual casualty. To the clinical recognition of wound shock the *Memorandum* devoted only half a page; therefore recent research has been greatly influenced by the obvious need for clearer definition. Such subsequent work starts at the admittedly great difficulty in the recognition of shock in its earliest stages, i.e. at the time when treatment is most likely to be quickly and completely effective. The chief difficulty has been that many patients may show pallor, low blood pressure, and an abnormal pulse rate without having been in the least 'shocked'. Shock should certainly be suspected when there has been severe injury, haemorrhage, or prolonged exposure, and suspicion becomes a certainty if, during careful watching, the above circulatory abnormalities increase rather than diminish. But this position may involve either delay in treatment of potentially severe cases or active treatment of patients who do not really require it.

PUBLISHED RECORDS ON SHOCK

With the above elements of uncertainty in mind, some surgeons have caused to be published a large number of records of individual cases. The two most carefully controlled series are (1) those of A. Kekwick, W. d'A. Maycock, H. L. Marriott, and L. E. H. Whitby, of the Army Blood Transfusion Service, published early in 1941; and (2) those of R. T. Grant and E. B.

Reeve, described later, in the same year. It may be well briefly to review these two papers as regards their presentation of transfusion methods in relation to resuscitation work. Both arrive at the same main conclusions and both give most useful diagnostic as well as therapeutic advice.

Kekwick, Maycock, Marriott, Whitby papers

Kekwick and his colleagues record the histories of 24 patients all of whom were either so severely injured that the presence of secondary shock was a practical certainty and transfusion was therefore instituted at once, or else their lowered blood pressure having failed to recover to 100 millimetres of mercury after an hour under rest, warmth, and morphine treatment, a clear diagnosis of secondary shock was held to be justified. The process of assessment in the second group is important. It obviously implies facilities for continuous observation of the patient's condition and this can be arrived at only by the institution, between the receiving room and the operating theatre and main wards, of a specially staffed and equipped 'resuscitation ward' in which the necessary period of observation can be allowed. As casualties arrive at hospital many of the patients may be placed at once in one of two categories, (1) those who are mainly frightened and shaken, and who exhibit simply the picture of primary shock already described, and (2) those so severely injured that secondary shock is inevitable. As the authors say, differentiation between primary and secondary shock is easy with extremes of injury, i.e. either when the wounding is of such severity that immediate transfusion is obviously required and delay would be dangerous, or when there are no wounds and transfusion would be both unnecessary and foolish. It is for the intermediate cases that systematic observation is essential, and the basic principle adopted in the series under review was that the degree to which rest in the recumbent, head-low position, combined with warmth and morphine treatment, produced improvement could give the best indication as to how far the immediate symptoms were due to primary shock. If after one hour the depressed blood pressure was still below 100 millimetres of mercury, the probability of secondary shock was held to be sufficiently great for transfusion to be begun. If, however, in that time the blood pressure had risen and stayed above 100 millimetres of mercury, it might be assumed that the shock was mainly primary, and that, so far as resuscitation went, transfusion would not be required, although it might be necessary during subsequent operations.

Fallacies in criteria

If observation of blood pressure variations alone is to be the main guide as to the need for transfusion, it is important to see what fallacies arise in connexion with the other possible criteria. The authors take them in turn as follows. As regards pulse, they found that before transfusion the rate did not appear to bear any constant relation to blood pressure, and that after transfusion the response of the pulse rate was far more irregular than that of the blood pressure. The mental state was not an index of shock or of its possibility of development. Degrees of pallor and cyanosis appeared to give no quantitative indication of shock. In all severe cases the patients had sub-normal temperatures and cold extremities but these signs were obviously influenced by external conditions. The amount of sweating was not constantly related to the degree of shock. Kekwick and his colleagues make a good case in fact for what might be termed 'control by blood pressure' with the use of simple haematological investigations to confirm physiological improvement and to decide upon the amount of fluid to be transfused. Roughly speaking, these workers found that a rise of 10–20 millimetres of mercury could be anticipated from every 540 cubic centimetres of fluid transfused, providing all factors causing loss of fluid had ceased to operate. They recommended that, plasma and blood being equally effective in restoring blood volume, with large transfusions 1 pint in 3 might be blood. It should be remembered that an approximately quantitative replacement of lost fluid is necessary, and that if operation is to follow or there is other reason to anticipate further blood or plasma loss, the machinery of transfusion should

be kept going, even though at reduced rate, so that further large volumes of fluid can immediately be given if necessary.

Other important points

A few other important points are brought out in the series quoted. Although the plasma used was from 10 to 56 days old and as much as six bottles were given in one case, there was no evidence of reactions due to old plasma, opalescent plasma, plasma with clots, or refiltered plasma. Blood and plasma were found to be equally efficient for restoring blood volume. As regards the possibility of aggravating by citrate transfusion the degree of alkalosis from which shocked patients may suffer, such estimations as were made showed that it was unlikely that citrate sufficient to be dangerous could be given during administration of the stored products now in use.

Subsequently the quantitative relationship between blood, plasma, and serum as regards blood volume restoration was dealt with by G. A. Harrison and L. E. R. Picken (1941) writing from the Regional Blood Transfusion Laboratory, Cambridge. They confirm the fact that lasting restoration depends upon successful replacement of dissolved protein previously lost from the circulation. The amount of such protein in the different blood products now in use must vary and therefore the optimum and maximum amounts transfusable also vary. The figures given for the maximum volumes which can be safely administered to the average patient are (in the Emergency Medical Services' bottles) serum 3.4, citrated plasma 5.1, citrated whole blood 8, and defibrinated blood 6.6. This result also gives workers a guide to the relative volumes of each likely to be required to produce any particular degree of restoration.

At this stage it might be regarded as established that the chief and constant feature of secondary shock is reduction of blood volume and that the most important single requirement for arresting progressive deterioration in the general condition is blood volume restoration, with resultant revival of tissue metabolism in general. Blood and plasma transfusions have justified their claims to be the best means of effecting this and, as emphasized earlier, the chief interest is now beginning to centre upon these observational factors which will allow the most effective as well as the most economical use to be made of transfusion.

Grant and Reeve papers

The findings in a larger series of cases (100) published by Grant and Reeve as a report to the Medical Research Council's Committee on traumatic shock carry matters a little further. Two points already made in the earlier series are again illustrated, viz. that even blood pressure readings may be misleading because (a) the originally hypertensive patient may suffer great blood or plasma loss without exhibiting a blood pressure below normal and (b) in a young previously healthy subject there may be so much compensatory vasoconstriction after blood loss that the blood pressure remains for some time above the normal level, with the apparent paradox that in such cases the pulse may be hardly palpable in spite of high blood pressure in the brachial artery. It is therefore important to remember when assessing the transfusion requirements of young subjects that their blood pressure is maintained better than the pulse factor, which in them may become a relatively important observation. Grant and Reeve also note that not only is concentration of the blood in shock very inconstant but also that there is so much variation in the rate of dilution after haemorrhage that haemoglobin estimations, even when 2 hours have elapsed, do not give any relative indication of the amount of blood lost; they agree that greater reliance can be placed upon blood pressure measurements. In order, however, better to define the therapeutic indications, these later observers divide their cases into three groups:

(1) This includes hypersensitive, often young, subjects who are first seen with good colour, blood pressure raised above 140 millimetres of mercury, and a relatively strong pulse, all of which may indicate absence of shock, or which may give an entirely false impression; in such patients, if wounds are

severe and blood has obviously been lost, collapse may be very sudden, and for safety's sake immediate transfusion is advised.

(2) In this group are those with a normal blood pressure (100 to 140). In many of these subjects, in spite of severe injury and haemorrhage, the blood pressure and pulse rate may remain normal and they are not very pale although they have suffered much loss of blood. They deserve close observation for a time, with rest, warmth, and morphine, so that if the pressure begins to fall and the pulse to rise, transfusion can at once be instituted. Again, however, if injury is so gross and haemorrhage so definite that clinical deterioration is probable, immediate transfusion is advisable.

(3) This comprises all those patients whose blood pressure when first seen is below 100 millimetres of mercury, and they are subdivided according to the pulse rates: (a) those with a slow pulse (under 70); they frequently improve markedly with rest, warmth, and sedatives; but in this series transfusion was found to be almost always necessary before or during operation; (b) those with a pulse between 70 and 100; these, the authors found, were only moderately improved by quiet and warmth, and all required transfusion treatment before definite and maintained improvement could be recorded; (c) those cases already showing a rapid pulse (over 100) and in which rest, warmth, and quiet alone always proved insufficient, and in some even transfusion failed to ensure resuscitation. From this it is clear that among the low-pressure cases, observation of the pulse rate serves a useful purpose even if at times its indications are unreliable.

Lessons to be learned

Commenting on the general conclusions to be drawn from their records, Grant and Reeve remark that on the whole, although there is usually some response to rest, warmth, and morphine, these measures are rarely sufficient once secondary shock has developed. Only in 17 of the cases in their series of 100 did the patients escape transfusion and in none of these was blood loss or the degree of injury severe. As regards the amount of transfusion required, Grant and Reeve agree that maintenance of a normal systolic blood pressure of at least 100 millimetres of mercury may be used as the chief index that sufficient blood, plasma, or serum has been given. The rate which they prefer is 1 pint in 15–30 minutes for initial pint transfusions, the rate being markedly slowed if further quantities are given. They find that, although any increase of speed has not an immediate bad effect, the resulting improvement in blood pressure is not so well maintained and further injury, such as may occur at operation, is not so well tolerated. Occasionally it was noted that the slow rate did not improve the pressure sufficiently quickly and the flow was then increased until, watch being kept on the blood pressure, the desired level was reached. Following this principle, most of the patients improved within a few hours, pallor and sweating decreasing and the blood pressure reaching the desired 100 millimetres of mercury. Meanwhile the pulse tended to return to normal whether the initial change had involved either a rise or fall in its rate. Of the unsuccessful cases it is noted that if on these lines improvement cannot be detected after administration of 2 or 3 pints of blood or plasma at a reasonable rate, recovery is unlikely.

TECHNICAL IMPROVEMENTS

As regards transfusion methods no basic changes have been made, only a few doubtful points made clear. The work of Maizels has been prominent in this field. If blood is to be transfused within 2 or 3 days, it is advisable still to use simple 3·8 per cent sodium citrate solution, 9 parts to 1 part of blood, because then minimal dilution obtains. For longer storage the choice is now 100 cubic centimetres of 2·5 per cent sodium citrate and 20 cubic centimetres of 15 per cent glucose to each 420 cubic centimetres of blood. The addition of glucose and greater dilution improve storage qualities, and such cells, even 10 to 14 days stored, nearly all survive in the patient and function normally. Although the stored red cells lose potassium, they are chemically reconditioned within 24 hours of transfusion. The liability of high

titre O plasma to agglutinate the cells of other groups has now been assessed. The risk is small unless the patient is very anaemic and his own cells already few. But whenever large volumes are to be given, it is advisable to use donors of the same group as the patient or else 'packed red cells' from which the plasma has been withdrawn. Transfusion of settled red cells without their accompanying plasma also has an advantage when it is not desired to increase blood volume; great oxygen-carrying power is provided in small bulk. But removal of plasma also removes the haemoplastic elements. Although plasma and serum keep, when stored wet, for very long periods, real permanence is obtained only by drying in vacuo. Plasma has no advantage over serum, in fact owing to its lower protein content larger volumes need to be transfused. There is no evidence that serum is more toxic than plasma; the latter is mainly used because it is so readily available from the blood banks.

CONCLUSIONS

As matters now stand, although it may be agreed that the underlying cause of the dangerous stage through which many patients pass is gross reduction in blood volume due to blood or plasma loss or both, yet 'shock' is still not a readily recognizable clinical entity. Nevertheless, the observations quoted clearly support the view that in the serious conditions implied in the description of secondary shock, the simple measures of rest, warmth, and sedatives are usually insufficient, whereas in patients received reasonably soon after injury, properly administered transfusions of blood or plasma are most effective in restoring and maintaining the circulation and promoting ultimate recovery. For the mild and average case those indications for transfusion based upon the blood pressure criteria given above are to be accepted as entirely workable. This is a decided improvement upon the early wholesale, often unnecessary transfusions of the earlier days of the war. But it is most important to realize that in the severe cases assessment of the need for immediate transfusion can more reliably be based upon the obvious severity of the patient's injuries and upon calculating as far as is possible the amount of blood he is likely to have lost. Although the criteria of shock already established may not present themselves for the moment, it is obvious that at any time this condition may supervene and, as Grant and Reeve remark, we should, in severely wounded cases with good evidence of blood loss, still begin transfusion regardless of other factors. It is evident that in this subject many fields are still open for yet further exploration, and since the work of the observers quoted above is being continued, their future publications must be looked forward to with great interest. (See also pp. 1 and 8.)

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CARDIOVASCULAR DISEASES

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In common with other departments of Medicine the present war has also assigned to cardiology its specific problems. For the most part these concern (a) the examination of military recruits and (b) invalidism within the fighting services from 'effort syndrome'.

Examination of recruits

The experience of examining a large number of young adults without symptoms is unusual in peace-time medical practice, and the work of Medical Boards, which is especially concerned with the early manifestations of disease, has emphasized the difficulty of recognizing heart disease at its inception and before characteristic physical signs make their appearance. Some recruits present obvious cardiovascular defects, but in others the true significance of certain findings is difficult to determine. Some of these problems are discussed below.

Exercise tolerance test

When an opinion has been passed on the state of the heart, grading of a recruit in this section of the examination is facilitated when it is appreciated that allocation must be made either to Grade 1 or to Grade 4. There is no room for Grades 2 and 3 in judging the efficiency of the cardiovascular system, so that the heart is either healthy (Grade 1) or faulty (Grade 4) and therefore unsuited for the exertion which is inseparable from any kind of military training. A healthy heart is unassailable by any degree of exertion even though considerable tachycardia may prevail at the time. It follows that any 'efficiency test' is purposeless if it only takes into account changes in the heart rate and respiratory rate after exercise and deliberately sets apart changes in the heart structure. The exercise tolerance test may well be an index of general physical fitness, but it is in no sense a yardstick with which to measure cardiac efficiency; a poor test may be recorded in a subject with a sound heart, while the performance of a heart enlarged from the effects of disease may often determine a satisfactory response.

A knowledge of the prognosis belonging to each separate cardiac lesion is the only reliable basis on which an estimate can be made of an individual's capacity for work and the probable effects upon the heart of added physical exertion. (See also p. 2.)

Signs of early mitral stenosis

Although absence of symptoms in mitral stenosis need not mean that the lesion in such cases is an early one, in many, if not in the majority, of recruits it is true. Thus, it would be useful to assemble a collection of physical signs which would establish the early diagnosis of mitral stenosis. The history of acute rheumatism or any of its manifestations, notably chorea, cannot help, for about half of the cases of mitral stenosis have no such story behind them, and almost the same proportion of patients presenting this past history escape heart injury. The pulse rate is valueless but its size is of considerable importance; if it is small it favours the diagnosis of mitral stenosis when the blood pressure is usually lowered as well. On the other hand, a pulse with a normal or even higher amplitude does not exclude the condition. The first sound in the mitral area in mitral stenosis is loud, but this is also true in the healthy and nervous subject, especially if tachycardia is a feature of the case, as is common in a great many recruits during the stress of examination. Thus a loud first sound in the mitral area, associated with a forcible heart beat in a patient not obviously nervous and without tachycardia, suggests mitral stenosis. The significance of a systolic murmur is dealt with in the next section. The intensity of the second sound in the pulmonary area offers no

help in the recognition of early mitral stenosis; it may be loud in a healthy heart, and normal or even subdued in those in whom a mitral lesion is proved to be present by other means. The electrocardiogram in relation to the diagnosis of early mitral disease is most helpful in the separation of congenital from acquired heart disease, although a chest lead may show a characteristic auricular wave in mitral stenosis. Cardioscopy is the surest means of discovering or confirming the presence of the early mitral lesion. A clue may come during screening in the anterior position, for the conus of the right ventricle may be prominent and associated with fullness of the pulmonary arc, but evidence of a distended left auricle in the right oblique position when viewing the left auricle impression on the barium-filled oesophagus, is the most certain indication of mitral stenosis. In this connexion it must be remembered that a shallow impression is a natural finding in health.

In practice therefore, whenever the diagnosis of mitral stenosis is in doubt, it is unlikely that any means apart from cardioscopy will decide the issue, and it should be resorted to in every instance.

The functional murmur

The mechanism of this murmur is unknown. Its importance is concerned solely with diagnosis from a murmur of organic heart disease. Some of its characteristics can be described, but there remain many cases in which an adherence to these criteria will miscarry in diagnosis. It is a sound precept first to gain a clinical impression of the murmur but never to attest to the diagnosis in the absence of an examination by cardioscopy. The following are the characteristics of the murmur: it is systolic in time and usually found in the mitral area, although sometimes it may also be present in the pulmonary area, especially when the person examined is in the reclining posture. It is seldom as loud or as substantial as the murmur of organic disease. Like the organic murmur, it may appear louder when the recruit is in the reclining than in the upright posture, but should the reverse be true, as often occurs, then the murmur is a functional one. It may become less intense with the phases of respiration and when tachycardia is induced. If the murmur occurs late in systole its functional nature is confirmed.

Normal blood pressure

The experience of recording, as a routine, blood pressure readings in recruits calls for a revision of the accepted figures for the normal blood pressure. In a healthy subject under 30 it is commonplace to find a systolic pressure of 160 to 170 millimetres of mercury when the diastolic pressure remains at 100 or under. The rise does not depend on tachycardia, and nervousness is presumably the cause, for there is no evidence of cardiovascular hypertrophy suggesting the presence of hyperpiesia. In practice these higher values of the systolic blood pressure are so common as to suggest the diagnosis of mitral stenosis in those with a systolic blood pressure of 115 to 120. Outward displacement of the apex beat in these subjects with a systolic blood pressure of 170 or so naturally leads to a consideration of hyperpiesia as the cause, but owing to the frequency with which scoliosis shifts the apex outwards, left ventricular hypertrophy must be proved by cardioscopy before the diagnosis of hypertension is substantiated.

Lessons for the future

The common incidence of doubt concerning the precise nature of certain physical signs elicited during the routine clinical examination of recruits, and the help gained in the solution of these problems by electrocardiography and more especially cardioscopy, supply serious lessons which must no longer go unheeded. The necessity for implementing clinical examination by the more specialized methods of examination is greatest in three principal circumstances. The first applies to the subject under discussion so that no healthy recruit shall be rejected on the grounds of suspicious cardiovascular signs, and that none with an obscure heart lesion shall be accepted for military service making him liable to invalidism both in the service and after demobilization. In the second place, no child, as the result of the customary school medical examination, shall be relegated to a sedentary life on the flimsy

evidence that there is a murmur in the heart. Probably a high proportion of school children are kept in bed for several months, or, if ambulatory, prevented from taking part in games and physical exercises, or are even allocated to special schools, on account of a cardiac murmur which cardioscopy would straightway establish as an innocent functional murmur. Thirdly, it is time to issue the warning that during demobilization of the members of the Services at the conclusion of hostilities none shall be awarded pensions in respect of uncertain designations such as D.A.H. and V.D.H. The experience is all too common of meeting in the course of routine clinical work combatants of the last war who have already received sums varying from £800 to £1,500 on account of alleged cardiac disability, but whose hearts in fact are healthy and who exhibit only innocent conditions such as extrasystoles or a functional murmur. There should be an early resolution that no combatant of the present war, discharged from the Services, is awarded compensation in respect of a cardiovascular fault unless the facilities of cardioscopy and electrocardiography have been made available during the clinical examination which apportions the award.

The effort syndrome

The diverse terminology applied to this symptom-complex is an index of its uncertain pathogenesis. Soldier's heart, athlete's heart, and neuro-circulatory asthenia are some of its other names. The last possesses the merits of directing attention away from the heart, because whatever hypothesis is brought forward to explain the nature of the disorder, one fact remains apart, namely that the heart is healthy. The numerous symptoms peculiar to the condition appear at odd times, but they are voiced most ardently during periods of stress. To review these periods in the life of a young adult is to make the condition better understood and help to allocate to it its true significance.

At school the patient's performance at games is as a rule indifferent, and partly on this account and because of a poor physique, the opinion of the School Medical Officer is often sought concerning the child's fitness. Exemption from games has sometimes turned the subject more closely to his studies, but more often he has chosen to relax and to seek ease and inactivity. Judicious management and encouragement at this stage by an understanding tutor have sometimes replaced his lack of self-confidence and vigour by a resolve to discharge creditably any responsibilities entrusted to him. More often, however, he has been left unnoticed to follow his inclinations and to come to believe more in his own infirmities.

In civil occupations, too, the patient continues to lack confidence and stamina whenever the opportunity is offered to display them. On occasion, and particularly when a test of will-power is imminent, or during convalescence from a slight illness, he seeks treatment from a medical officer, who may prescribe reassurance together with a sedative medicine, but more often the heart comes under suspicion because of the nature of the presenting symptoms conjoined with the finding of a systolic (functional) mitral murmur, and the foundation of cardiac neurosis is thereby cemented.

It is during the medical examination preliminary to, or in the course of, military training that this symptom-complex looms prominently. The symptoms on this occasion receive emphasis by the recruit or combatant, and they claim unusual attention from the examiner, who has found that routine investigation of young adults has assembled a group possessing a common symptomatology. In assigning such candidates to a category representing fitness for active military training it is necessary to be aware of the fact that they seldom develop into staunch combatants, for they are temperamentally unsuited to the calling, and from the start they are unequivocally opposed to the proposition confronting them. Although the aim of treatment should always be directed towards creating within the individual that measure of will-power which will give him mastery over himself and his difficulties, the possibility of attaining this end is slender. Indeed it may be necessary, in order to relieve the symptoms, to withdraw the circumstances which have

precipitated them, even though weakness and instability would appear to be in this way rewarded and even encouraged.

Conclusions

The time then is long overdue for a proper appraisal of the collection of symptoms under discussion. The physician should not be hoodwinked into the belief that they might be the outcome of organic disease, particularly of the heart. Rather should they be known for what they stand, namely an expression of fear in the face of trials, and a desire to evade rather than surmount them.

CHILDREN'S DISEASES

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In any survey of the past year's progress in paediatrics pride of place must be given to the therapeutic weapon afforded by the sulphonamide group of drugs. These are discussed first; after which a summary of recent work on vitamins as it affects prevention and treatment of disease in childhood is given. Lastly, the time is ripe for a survey of the medical and surgical methods of treating congenital pyloric stenosis.

THE SULPHONAMIDES

Dosage and tolerance

These drugs offer just as much scope for therapeutic success in childhood as in the adult. Dosage needs some special consideration and, on the whole, it is easier to relate this to the child's age rather than to bodyweight. The aim is to secure a concentration in the blood of 4 to 10 milligrams per 100 cubic centimetres and to hold it at this level for three or four days. M. Hynes (1940) has worked out a useful scheme of dosage which secures this (see table). In general, children stand the drugs well; there is surprisingly less vomiting with sulphapyridine as compared with the effect of this drug in adults, and if intense mental depression occurs, young children at any rate do not appear to be in a greater state of misery than would be accounted for by their original illness.

Table of Sulphonamide Dosage

AGE	DOSE IN TABLETS (1 TABLET = 0.5 GRAMME)	DOSE IN 24 HOURS (GRAMMES)
0 - 3 months	$\frac{1}{4}$ 4-hourly	0.75
3 - 6 "	$\frac{1}{2}$ 6 "	1.0
6 - 18 "	$\frac{1}{2}$ 4 "	1.5
$1\frac{1}{2}$ - 4 years	1 6 "	2.0
4 - 8 "	1 4 "	3.0
8 - 12 "	2 6 "	4.0

The first dose should be double that of the rest of the series.

Possible dangers

The possible dangers of sulphonamide certainly exist in childhood, and as might be expected the blood-forming tissues can occasionally react unfavourably. A case of agranulocytosis in an infant with recovery has been recorded by H. C. Barlow (1941). Sulphapyridine was given to a two-year-old girl with otitis media in a dosage of $\frac{1}{4}$ tablet (0.125 gramme) twice daily for five days. This led to a profound anaemia (the haemoglobin sank to 18 per cent) and disappearance of all polymorphonuclear cells. Transfusion and pentnucleotide, however, effected a cure after a stormy time. The dosage was small, and the possibility of a hypersensitivity phenomenon has clearly to be considered. (See also p. 6.)

Clinical records

Good surveys of the value of the sulphonamides in the infections for which they are commonly used have been given by A. M. Gill (1940) in the case of pneumonia in infants under 1 year (7 recoveries out of 11 severely ill babies) and by Margaret I. Williams (1940) for cerebrospinal fever with a total case mortality in 102 children of 12.7 per cent. Williams used a suspension of sulphanilamide powder in a dosage of 0.08 gramme per pound of body

weight per day for ten days. Mary Moffett (1940) has indicated the value of sulphapyridine in gonococcal infections in childhood, her most successful results being obtained in gonococcal ophthalmia, for which she gave $\frac{1}{4}$ tablet four times a day crushed in milk with a pinch of sodium bicarbonate, combined with local irrigation with normal saline every four hours. Smears were usually negative within four days and the drug was stopped 48 hours later.

Sulphathiazole

Of the most recently available member of the series, sulphathiazole, there are naturally few reports available. An encouraging account by D. H. Paterson and A. J. Walker (1940) of an infant with osteomyelitis and severe pericarditis following styes (and presumably of staphylococcal origin) successfully treated with this drug holds out possibilities that yet another type of serious infection can be attacked.

Poliomyelitis

On the whole the sulphonamides have proved of little value against virus infections, but an interesting account of an outbreak of poliomyelitis treated by convalescent serum and sulphapyridine in combination holds out hope that even this type of infection can be brought under control. S. Miller and S. Wray (1941) in reporting this result, based on a study of 75 cases, assert that the attacks were rapidly controlled by sulphapyridine, either alone or with convalescent poliomyelitis serum, together with other appropriate treatment.

Rheumatic fever

In rheumatic fever, despite the possible aetiological part played by the haemolytic streptococcus, the sulphonamides have proved of no value in treatment, and indeed are believed to be harmful. On the other hand, in the prophylaxis of rheumatic fever a strong case has been made for the use of sulphanilamide by workers in America (C. B. Thomas, R. France, and F. Reichsman, 1941). The drug was given daily to children under supervision for rheumatic activity in two doses of 0.6 gramme for the whole of the 'winter-cold' period, October to June. No major rheumatic attacks occurred in 55 children thus treated, whereas in a control group of 67 children there were 15 such attacks. No deleterious effects were observed and the children led ordinary lives, so that it would appear that the drug does in some way repress rheumatic activity.

VITAMINS

Problems of nutrition loom large in war-time and it may be that a better knowledge of the subject will spread among the public. Perhaps even new work may be done, comparable with the classical studies on rickets made in Vienna after the war of 1914-18. Of all nutritional problems those concerned with vitamins are most serious. The fat-soluble vitamins A and D are of great importance, and with fish-oil supplies diminished, synthetic preparations in arachnis oil are being made available. Every piece of scientific evidence warrants this emergency measure. (See also pp. 5 and 120.)

Vitamin C

Vitamin C in war-time has presented special problems because of shortage of oranges and tomatoes, both favourite sources of this vitamin for young children and particularly important with the modern increased use of dried milk and proprietary milk foods in infant feeding. Ascorbic acid is available in tablet form and is reasonably cheap, but the best solution of the problem in the infant is to plan for the introduction of mixed feeding at six months of age with a plentiful use of potatoes, swedes, peas, and cabbage as additions to the 'bone and vegetable broth'. Whether or not older children are likely to suffer from vitamin C deficiency still remains debatable. Certainly overt scurvy is seldom seen after the first year of life, but using special tests, workers have claimed that diets in the poorer classes are likely to be lacking in vitamin C. Thus N. U. Khan and M. Minn (1941) report a survey of children in Newcastle-on-Tyne using the capillary resistance test as a gauge of vitamin C defect. Children of good nutrition from a private school were all

negative to the test, but among children living in the poorer parts of the town a certain number of abnormal cases of decreased capillary resistance were found, 7 out of 8 returning to normal after being given 100 milligrams of ascorbic acid daily.

Vitamin B₁

Vitamin B₁ has been used in the treatment of 'pink disease' and is best given by intramuscular injection in doses of 2 milligrams every other day, a drop in pulse rate being a striking proof of the success of the therapy in some cases. But the effects are curiously variable and in Australia G. Forsyth (1941) has reported good results with wheat-germ oil (several capsules a day) after a vitamin B preparation had failed to improve a child who had had a relapse. M. R. Price (1940) has also stressed the importance of vitamin B₁ in promoting optimum growth in infants and claims good results with a tablet of pulvis vitamin B₁ (*British Pharmacopoeia Addendum*) in a dose of 100 international units daily.

Vitamin E

Vitamin E has been recommended for the treatment of muscular dystrophies, this form of therapy being based upon experimental work in animals. The most spectacular results are those reported by F. Bicknell (1940), who used fresh dried whole wheat-germ, giving $\frac{1}{2}$ ounce twice daily; every patient save one out of 18 cases of myopathy treated for over six weeks showed definite improvement.

Vitamin K

From the work of H. Dam, E. Tage-Hansen, and P. Plum (1939) it is now clearly established that vitamin K is necessary to counteract the fall in blood-prothrombin levels which occurs after birth in all babies, producing the dangerous 'haemorrhagic disease' of the new-born in some. It is now clear that a synthetic analogue of vitamin K (a naphtha-quinone derivative) achieves the same result, and recent work has suggested that given to mothers not less than four hours, or more than twelve, before expected delivery, the fall in the prothrombin level of the new-born baby's blood can be prevented. The dose recommended is 10 to 15 milligrams of the synthetic vitamin K analogue intramuscularly. It has been urged by some workers that this should be a routine procedure in all deliveries. It should certainly be used if there is a history of a preceding child having suffered from any variety of neonatal haemorrhage and in all cases of difficult labour and for all premature deliveries. The vitamin K preparation can also be used therapeutically when a new-born baby begins to bleed from any situation (see especially G. P. Bohlenden, W. M. Rosenbaum, and E. C. Sage, 1941). (See also pp. 5 and 122.)

CONGENITAL PYLORIC STENOSIS

With the introduction of Rammstedt's operation of pyloroplasty the treatment of pyloric stenosis in infants had become almost entirely surgical, at any rate in the United Kingdom. Medical treatment, however, has come in again with the introduction of eumydrin (atropine methylnitrate) by E. Svendsgaard in 1935.

Eumydrin

Recently reports by Helen M. Mackay (1941) and R. H. Dobbs (1941) on the use of eumydrin have produced in each instance a series of 40 cases with 5 deaths, and both authors have claimed this as a great advance on surgical procedures, for which they put the mortality rate at about 25 per cent. Eumydrin treatment consists essentially of the use of a freshly prepared aqueous solution, 1 in 10,000, and the administration of 1 cubic centimetre before each feed, increasing up to even 5, 6, or 7 cubic centimetres until vomiting is controlled. Dobbs favours gastric lavage in addition; but Mackay doubts if this gives any added benefit. A possible variation is to use an alcoholic solution of eumydrin, as suggested by A. Wallgren (1940), who applies one drop of this (0.6 per cent in strength) on the tongue once or twice a day. The figure of 25 per cent for surgical mortality is probably unfairly high; D. Levi (1941) has

promptly attacked the statement with a report on a consecutive series of 100 breast-fed babies all operated upon under local anaesthesia without a single death and a similar series of 46 bottle-fed babies resulting in 5 deaths, all from gastro-enteritis. The 'eumydrin school' would no doubt reply that such results are achieved only in a special hospital by an experienced surgeon and a first-rate team, but it seems equally clear that treatment by eumydrin, especially if gastric lavage is included, requires skilled nursing and careful supervision, so that it is fair to compare the best results of both series, which undoubtedly gives a verdict in favour of surgery so far as the United Kingdom is concerned. It is clear that the length of stay in hospital is an important point, for as things are this often means an increased risk of infective gastro-enteritis, acquired in an open ward. Moreover if breast-feeding is to be continued—and it is always to be desired, as there is an overwhelming decrease of risk in the breast-fed—economic and social reasons necessitate that the time spent in hospital should be reduced as much as possible. Until the eumydrin treatment can be applied to out-patients, or at any rate until it can be continued in the out-patient department after a week or so of hospital treatment, it would appear that an infant with pyloric stenosis stands the best chance of recovery if taken to the nearest surgical centre for operation. A study of the subject also makes it only too unfortunately clear that cross infection in the wards of an infants' hospital represents a serious problem, and not only in regard to pyloric stenosis. Drastic steps must be taken to deal with this in the future. (See also pp. 4 and 13.)

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EAR, NOSE, AND THROAT DISEASES

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PSYCHOLOGICAL EFFECTS OF DEAFNESS

The effects of deafness upon persons of varied mentality differ, but there is also another fundamental difference according to whether the deaf person has possessed normal hearing in youth, has possessed it only for a few years, or has never heard clearly at all. That is to say, the reaction to deafness of congenital type, in which rubric for clinical purposes deafness acquired early in life is included, is different from the reaction to the deafness which is felt as a loss by an individual who has to a great extent received impressions of the external world, has acquired his education, and has experienced much of his enjoyment of life by the agency of the sense of hearing. Deaf-mutes who cannot feel the loss of a sense they have never known are therefore almost in a class apart, and it is necessary to consider separately the effects of deafness originating (a) in childhood and (b) in later life.

It is to be expected that, just as in those who become deaf later in life, character and personality vary amongst those deaf from birth or from an early period, and they are unlikely to form a mentally homogeneous group. Nevertheless A. Eichholz (1932) stated that during the period of childhood, given an early commencement of education, practically no problem of temperament arises. Deaf-mutes are happy in their own company, and only among those who do not show sympathy and understanding do they feel isolated and become morose, dissatisfied, and depressed. The child reaches the limit of school age, contented, responsive, capable, and ready to take his place as an active worker in the world. At this moment the deaf-mute probably reaches the zenith of happiness. He leaves school at 16 ready and even anxious to face the world. When the novelty of work wears off or adverse conditions of employment arise, altered circumstances may react seriously upon his attitude and behaviour. These changes do not begin at once, but usually within 2 to 4 years of leaving school, that is at about the age of 18 to 20 years. This, however, is only the normal reaction of anyone who happens to find himself in uncongenial company, and accounts for the conflicts which occur in relations with normal people who lack the inclination or capacity to establish harmonious contact with the deaf-mute.

Education

The need for beginning education as early as possible is clear, for those beings, deprived of the capacity to acquire knowledge and communicate their thoughts in the normal manner, must inevitably be difficult to manage until means of receiving impressions and instructions and of expressing thoughts and desires have been acquired. According to Irene Ewing (1941), fear and mental conflict are common in young uneducated deaf children, and she has found great difficulty in pacifying and calming such children who have experienced terror in a dream. Mainly through touch can the sense of security be restored. The comfort of words and the sound of a familiar voice are denied to these children.

Formerly compulsory education for the blind began at 5 years of age, whereas for the deaf the age was 7. In 1937 the age for the deaf was lowered to 5 by Act of Parliament. This step, which placed the deaf and blind on the same level in this respect, was urged for many years by the National College of Teachers of the Deaf and by the National Institute for the Deaf with the support of Eichholz; in a few years its beneficial effects should become apparent.

As the development of the mind largely depends upon the acquisition and development of speech, and both in turn depend upon the ability to hear, even a slight degree of deafness at any time during childhood retards both the powers of comprehension and the acquisition of normal speech. Severe or total deafness in childhood makes it impossible to acquire normal speech. The mental life of the child is also affected by his inability to think in words, to hear those directions and explanations which regulate his conduct in a world without reason, and to play freely with other children. His interests are mainly confined to what he can see, and the urge to give expression to his emotions and thoughts is repressed by lack of the normal outlet.

Irene Ewing mentions a lady pupil who had been born deaf and had not been given any opportunity of education. She had lived apart from other deaf people and had to rely on gestures as her sole means of communication with others. She knew no word of English or of any other language. She could play a good game of whist, yet she did not know the names of the cards nor could she count by any ordinary means. She had learned the game simply by watching others play. It is difficult for a hearing person to form any conception of the mental processes of one with this limitation.

Some deaf children are slow in learning to walk, possibly because, owing to a congenital defect of the labyrinth, they lack the sense of balance, but also because when learning to walk with the help of a chair the words of encouragement and the sound of the mother's voice are missing, there is no incentive to progress, attention is centred on the chair, and interest in walking soon fails.

All this enforces the urgent necessity of beginning the education of the deaf child without delay and in the right way, for these children labour under a severe handicap. How successfully education can be accomplished is shown by the statement of Eichholz that their isolation from the hearing world does not prevent deaf-mutes from entering successfully into all the ordinary activities of life. They marry among themselves and occasionally, with hearing partners, found good homes, enter practically every industry for which hearing is not required, engage in sports, and generally lead the life of normal persons. They have the reputation of great power of concentration because they are not easily distracted from the work in hand. It is, however, admitted that this satisfactory picture is by no means universal, and the interaction between the defect of hearing and some incidental minor defect of character or personality often prevents the deaf-mute from adapting himself to the ordinary conditions of social life. In this way instability of temper, petulance, aggressive and even violent conduct arise, and, still more serious, mental abnormalities, such as depression, melancholia, and actual insanity with homicidal or suicidal tendencies, may follow. Eichholz stated that the incidence of insanity amongst deaf-mutes is 1 : 42, as compared with 1 : 295 among the general population. H. Frey (1941) gives a plausible explanation of the apparently abnormal conduct of some deaf-mutes. The reaction to unfriendly surroundings is really normal, and only appears abnormal on account of the difficulty which the deaf-mute finds in expressing himself. He cannot in the normal way give his opponent 'a piece of his mind' in speech and relieve himself by the usual outlet of speech in the form of complaints or abusive language, and his limited powers of self-expression drive him to resort to physical violence.

Mental capacity of deaf-mutes

There are among deaf-mutes many abnormal persons apart from their deafness; they are degenerates not only in the development of the hearing organ but in other respects. Thus Eichholz stated that in a review of mental capacity 18 per cent of deaf-mute children were found to be mentally backward and 4 per cent mentally defective. This suggests that congenital deaf-mutism is more likely to be associated with mental abnormalities than deaf-mutism arising from deafness originating in early childhood from an accidental cause such as cerebrospinal fever. The diagnosis of deafness in childhood, however, is not always easy. The common mistake lies in confusion

between deaf-mutism and mental deficiency. A child who fails to respond to the spoken word may be classed as mentally defective, when he is really a mentally normal deaf-mute. Congenital motor aphasia with normal hearing and mentality may cause a similar error, but the condition is rare. To avoid these mistakes, tests of intelligence for the deaf and dumb have been devised which exclude any talking. They are called 'performance' tests, because the child has to do something usually in the nature of fitting together the pieces of a puzzle. The detailed application of this requires training in psychological and vocational therapy, but it is highly important to observe the principle, because its neglect may deprive the mentally deaf child of proper educational advantages.

The story of Helen Keller, who became both blind and deaf before the age of 2 years, is evidence that even the combination of these defects need not have any ill effect on either the character or the mentality. The miracle of her education by Anne Sullivan, which did not begin until about the age of 7, produced a personality far above the ordinary level of intellectual attainment. According to J. K. Love (1936), who knew Helen Keller well, the impressions received during the first few months of life while the senses of sight and hearing were fully receptive made this possible.

It seems, therefore, that deaf-mutism or a severe grade of deafness in childhood does not necessarily have any gross psychological effects as a simple consequence of the hearing defect if the problem of education is not neglected; that limited means of self-expression sometimes produce reactions which, though they may appear abnormal, are not due to defects of character but are normal reactions to abnormal conditions of life, for deaf-mutes live happily amongst themselves and do not mind their deafness; but that many congenital deaf-mutes are degenerates in other respects, both physically and mentally, and this rather than deafness alone explains a high percentage of mental disorder amongst such people.

Later deafness and the mind

A different effect is found in those who become deaf later in life. In the first place, some people who become deaf still continue to enjoy life and do not complain of their deafness. There are not many such, but they are numerous enough to show that some psychological effect is not a necessary sequence of deafness which supervenes after a general knowledge of life, education, and normal mental activities have been acquired through the sense of hearing. Such adults have the advantage that their intellectual capacity and efficiency are established, whereas in the child the development of these is interrupted by deafness, and the question which presents itself is whether there is any specific psychological reaction to deafness or whether the reaction may be any one of those that follow any organic disability. A. B. Stokes (1941) states that whatever the disability may be, the psychological response will be one of relatively few and not specific for any particular disability. Thus there may be an anxiety response, or a depressive response, or a hysterical response, or a paranoid response to the onset of blindness, but the same behaviour patterns are encountered in patients who have lost a leg or have a weak heart. Moreover, the pattern of reaction associated with the organic disability can be traced back, so that it can usually be recognized as a component of the personality, in existence though less conspicuous before the disability became established, but showing itself as a florid response to the hardship and stress occasioned by the disability.

A particular organic disability may naturally pick out an individual to whom it is a special hardship, so that the precise form of the psychological response is decided by the combination between the personality of the individual and the nature of the organic defect. Thus a blind man inclined by nature to be suspicious may become paranoid from his blindness and believe that people are gazing and sneering at him or obstructing him. In the same way deafness may produce anxiety, hypochondriasis, or depression according as the individual has been previously apprehensive and timid, self-centred, or gloomy. In the shy, retiring, sensitive person, who easily withdraws into his shell and

cannot endure criticism, deafness may precipitate a schizoid response, or the response may be hysterical, obsessional, or paranoid according to the character of the individual. The nature of the difficulties which arise from hardness of hearing, which impedes conversation and is apt to exclude the deaf from society, is particularly likely to produce a paranoid reaction in a susceptible person who is already inclined to regard his fellows with hostility. His deafness then makes him believe that all conversations which he cannot hear are about himself, and that his faults and failings are being shouted abroad. Stokes, however, is of the opinion that deafness is not commoner among paranoid patients than it is among the general population, the personality factor being fundamental.

Influence of mode of onset

The mode of onset of deafness is likely to play an important part in the psychological reaction which follows. Deafness of sudden onset, especially of perceptive type as might follow cerebrospinal fever, labyrinthitis, or injury, comes as a severe psychic shock, whereas progressive hardness of hearing, such as that which is caused by otosclerosis and affects the conducting mechanism primarily, is more open to compensation and adjustment. The former is liable to produce an affective response, either anxiety or depression, but especially a hysterical state in which a transient deafness may be perpetuated as a functional condition. This is well known to follow the blast of an explosion. N. R. Blegvad (1937) regards this as the usual cause of persistent deafness following a loud noise or an explosion. In deafness of gradual onset the patient has a better chance to adjust the mode of life and to compensate for the loss of hearing by learning lip-reading or adapting himself to the use of a suitable hearing aid.

Effect of certain lesions

The type of aural defect is also important, whether it be of middle ear type with retention of hearing by bone conduction, or of internal ear type with deafness of high degree and loss of hearing by bone conduction. In the first case the patient can still hear his own speech by bone conduction, and therefore continues to speak intelligibly. External masking noises are inaudible or much reduced, and hearing his own voice above them he thinks he is talking very loudly and lowers his voice. In consequence, when others raise their voices in a noise, he fails to accommodate his own voice in the same way, and finds conversation in such conditions difficult. Some with middle ear deafness shun meetings and large gatherings for this reason. This kind of deafness is open to compensation by lip-reading and the use of hearing aids, so that psychological and isolating effects can be mitigated or avoided and a full happy life is possible. Margaret Monro, in *Breaking Out of Prison*, has well described how the subject of a severe type of this form of deafness can be rescued if the situation is faced with determination by the patient and with genuine sympathy by the relatives.

Internal ear deafness is even more serious in its secondary effects. The perceptive mechanism is impaired and there is loss of bone conduction, so that the patient can no longer hear his own voice. He may raise his voice in the effort to make it audible to himself, and such patients sometimes shout in contrast to those with otosclerosis who speak in low tones. If the patient tries to reproduce speech as he hears it he may on the other hand speak quietly but indistinctly and his own speech is then likely to deteriorate rapidly, because he cannot hear it. In this form of deafness the upper tones are lost. This renders speech unintelligible to the deaf or only intelligible with difficulty, the loudness being not much reduced because the lower tones are preserved. Consequently all speech is not only less intelligible but is distorted, and the distortion is increased by the use of a hearing aid. If this be so, lip-reading is the only resource, and conversation can be conducted if at all only in quiet surroundings. Children acquire lip-reading easily, whereas older people learn it with increasing difficulty, but in the case of internal ear deafness the effort should be made. Irene Ewing mentions the case of a cotton operative who became deaf from cerebrospinal fever at the age of 32. He was told that if

he could learn lip-reading in three months he could keep his job. Here again the situation was faced with courage, the condition was fulfilled, and the man retained his job.

Beethoven's deafness

When lip-reading cannot be acquired, the threat to the mental life in such conditions is grave, and is well illustrated by the story of Beethoven.

Much has been written, though but little in English, of the subjective experiences of Beethoven, who was born at Bonn in 1770 and began to grow deaf in 1796. His sufferings related in some of his letters and in the celebrated Testament of Heiligenstadt, the will which he made in favour of his brothers Carl and Johann in 1802, are typical, though obviously the patient was no ordinary person. The exact nature of the deafness has not been determined, as the temporal bones which were removed at the necropsy in 1827 were lost, but it was observed that there were gross changes in the auditory nerves. By the end of 1815 he had become totally deaf and from that time those who conversed with him had to do so by writing on cards which he carried with him. At first he tried to conceal his deafness, and was so sensitive about it that his friends had to be careful not to speak too loudly and so show that it had been noticed. In 1800 he wrote to a friend:

'You must know that the finest part of me, my hearing, has become very feeble. . . . My hearing, will it get better? Naturally I have hopes, but it is very difficult, because such maladies are amongst the most incurable. . . . What I have told you about my hearing, I beg you to keep a close secret, and confide to no one whatsoever.'

To another he wrote in 1801:

'I am better and stronger, it is only that my ears buzz and roar night and day. I lead a miserable life. For nearly two years I have avoided all company because I cannot say to people—"I am deaf." If I followed any other profession, it might be possible, but in mine the situation is terrible. What will my enemies say about it, and they are not a few? To give you some idea of this strange deafness, I must tell you that at the theatre I have to sit quite near the orchestra to understand the performers. I do not hear the high notes of instruments or of voices, if I place myself a short distance away. It is surprising that in conversation there should be people who have never noticed it. When people speak low, I scarcely hear, or rather I hear the sounds, but not the words, and yet if anyone shouts I find it intolerable. . . . Often I have cursed my existence and my Creator. Plutarch has taught me resignation. I wish that it may be possible to face my destiny, but there are times in my life when I am God's most miserable creature. I beg of you to tell no one of my condition, and I confide this to you under the seal of secrecy.'

From another letter in 1801:

'You can scarcely believe what a life of solitude and sadness I have led for the last two years. My infirmity rises before me like a spectre and I flee from mankind. I must appear a misanthrope, which is the last thing I am. . . . If only I were free from this malady, I would embrace the world.'

He contemplated suicide: 'If I had not read somewhere that a man must not voluntarily give up his life so long as he is capable of doing some good, I should long ago have been no more and doubtless by my own act.'

In the Testament he wrote similar accounts of what he suffered: 'For six years an incurable disease has struck me, and it has been aggravated by stupid doctors. Disappointed year after year in my hopes of improvement, forced to face a permanent disability, I have, though of an ardent and lively disposition, soon been forced into isolation and a solitary existence. . . . I cannot say to people, "Speak louder, shout, I am deaf." . . . My lot is doubly hard, because I am misunderstood. I find no distraction in the company of others, there are no interesting meetings, no mutual exchange of thoughts. I have to live like an exile.'

Yet Beethoven was able to rise above his sufferings and some of his most celebrated works, including the Ninth Symphony, were composed when he was totally deaf. G. Canuyt (1923) has tried to show that his deafness carried him away from the realities of life, that music as a kind of abstraction, apart from the sense of hearing, became possible to him, and thus he was capable of compositions which have transcended all others. This view seems fanciful and it is nearer the truth to say that the spirit of Beethoven was such that he triumphed in spite of his deafness.

CHEMOTHERAPY IN OTOTOLOGY AND LARYNGOLOGY

The drugs of the sulphonamide group, such as sulphanilamide and sulphapyridine, have now been subjected to a prolonged clinical trial and this is therefore a suitable time to take stock of the position, especially in otology,

where their use is of much value, but equally demands great caution. Although it is a great advantage to have some standard indications for their use and some settled procedure in ordinary clinical routine is essential, this is far from suggesting that a stationary position has been reached, for new drugs are constantly being produced, and at present it seems that sulphathiazole (M & B 760) will prove to be more powerful against the pneumococcus and less toxic to the host than sulphapyridine (M & B 693), and it is hoped that it will prove effective against the *Staphylococcus aureus*. Other sulphonamide drugs, such as sulphadiazine, are also in process of testing.

Acute otitis media

In acute suppurative otitis media it is now established that chemotherapy can cut short the disease and that its use materially lessens the incidence of complications. Because otitis media usually runs a short course, E. P. Fowler (1940) recommended that chemotherapy should be withheld at the onset, and should be reserved for cases in which at the end of seven or ten days patients have not made satisfactory progress under the usual treatment. This recommendation certainly draws attention to the need for close and continued observation during the administration, but its routine adoption would fail to take full advantage of the powerful effects obtained in the initial stages of the disease. W. C. Bowers (1940) made observations on 793 cases, of which 396 were treated by chemotherapy. In treated cases the duration of the aural discharge was on the average reduced by 50 per cent and the number of mastoid operations was reduced by the same amount, in comparison with the untreated cases of the series. V. G. Horan and S. G. French (1940) also record a series of cases from 1934 to 1937 before the treatment was introduced and a series from 1937 to 1939. The table shows the results:

YEARS	NO. OF CASES	MASTOID OPERATIONS	PERCENTAGE OF OPERATIONS
1934-7	607	138	22.7
1937-9	621	21	3.4

It is also significant that there was no fatal case in the second series, whereas there had been several deaths annually in previous years. This record affords particularly convincing evidence of the value of sulphanilamide because the number of cases is about equal in the two series, the numbers are large, and the clinical material is of a homogeneous character, being drawn from the Royal Navy.

Experience, however, has shown that this method of treatment is not so simple as some have supposed from reports of this kind and from the observation of a few cases of rapid recovery under the administration of sulphanilamide, generally in the form of prontosil. If the most is to be gained from this powerful aid, bacteriological examination is essential, for without it the treatment becomes merely empirical.

The incidence of different causal organisms varies in the records of different observers and in the course of different epidemics. In about one-third of the cases the haemolytic streptococcus is found, in about one-third the pneumococcus, usually but not always with a large preponderance of Type III as B. Hansen (1940) has shown, and the remaining third consists of infections by the *Staphylococcus aureus* and other occasional pyogenic organisms including the *Staphylococcus albus* and *B. coli*, *B. proteus*, and *B. pyocyaneus*. It is probable, however, that the true proportion of streptococcal infections is much higher, and that the results of laboratory investigation depend very much on the method of collecting the specimen for examination. In cases which come to operation with the opportunity for obtaining infected bone or pus direct from the mastoid cells a great majority of the infections prove to be streptococcal, about one-fifth to one-quarter pneumococcal, and a very few due to the *Staphylococcus aureus*. The large proportion of staphylococcal infections reported by some writers, even up to 40 per cent, seems to be due to contamination and overgrowth of the cultures by organisms from the skin of the external auditory meatus, when the specimen is taken from the aural discharge.

cerebrospinal fluid yielded a positive culture of pneumococcus, but did not give any clinical response to oral administration or to intramuscular injections. The child recovered after 4 intrathecal injections of 20 cubic centimetres of neococcy combined with administration by the mouth. It seems, therefore, that in a few cases the meninges are impermeable to these drugs, though usually the concentration in the blood and the cerebrospinal fluid is almost the same, being slightly higher in the blood. Any pronounced differences are rare, but R. Martin and his colleagues (1940) investigated this question and found that in one case the concentration of the drug reached 7 milligrams per cent in the blood, remaining, however, at 1 milligram per cent in the cerebrospinal fluid. As a concentration of not less than 4 milligrams per cent is required to produce a therapeutic effect there is a strong case for intrathecal injections in such circumstances. Injection might also be used in severe or advanced cases in which it is urgently necessary to reach a high concentration in the cerebrospinal fluid rapidly. Martin has shown that during administration by the mouth after 24 hours the concentration reaches 3 milligrams per cent, after 48 hours 4 milligrams per cent, and 6 milligrams per cent after 3 days. On the other hand the drug diffuses out of the fluid very quickly when injected intrathecally and falls to the blood concentration in about 9 hours, keeping a fairly high concentration for about 6 hours only. Assuming that the total quantity of cerebrospinal fluid is 150 cubic centimetres, Martin has made this calculation. If some cerebrospinal fluid is withdrawn by lumbar puncture and replaced by 20 cubic centimetres of a neutral 0.85 per cent solution, a concentration of 113 milligrams per cent is then given. If 5 milligrams per cent is already present from administration by the mouth, a concentration of 118 milligrams per cent is reached in the cerebrospinal fluid. This, however, soon falls to blood concentration, so that the intrathecal injections should be given twice daily. No ill effects, such as pareses or other sequelae have been observed to follow the use of this weak solution, but it would probably be dangerous to employ any higher concentration.

Septic thrombosis

The same principle applies to the control of venous infections arising from septic thrombosis. It is not sufficient to control the septicaemia with sulphanilamide, which only masks the underlying disease until the clot disintegrates and the patient succumbs from the effects of septic embolism in the lungs and elsewhere. It is necessary to remove the infected clot at the time of operation on the mastoid, and if the clot has extended downwards out of reach into the bulb, the jugular vein must be tied and divided in the neck to prevent embolism. The upper end of the vein can be brought out of the wound and left hanging outside the neck. When the ligature is removed this provides drainage for the clot breaking down in the bulb. In short, undrained pus and infected clot must receive attention on established surgical principles if the full benefit is to be derived from chemotherapy. To achieve success not only is it necessary to ascertain that a specific drug is available for the particular infection in question, but attention must be given to the dosage, which must be sufficient in both quantity and duration. Fowler observed that out-patients treated with a small or short dosage showed no more tendency to recovery than those of an untreated series. When the drug has no effect, the dosage is usually inadequate, and often there is a recurrence of symptoms if an adequate dosage is not prolonged for a few days after the temperature has fallen to normal.

In order to bring the patient under the influence of the drug rapidly it is recommended that the initial or loading dose should be double, so that a high concentration is reached quickly in the blood. The drug is dispensed in tablets containing 0.5 gramme. The initial dose is 2 grammes (4 tablets) followed by 1 gramme (2 tablets) four-hourly for 36 hours. Then 0.5 gramme (1 tablet) is given four-hourly for 24 or 36 hours. Finally 0.5 gramme (1 tablet) is given eight-hourly for 2 days. The total dosage is about 20 grammes. The dosage should bear some relation to the weight of the individual. For children the following dosage is suggested four-hourly:

AGE	1-3 MONTHS	6 MONTHS-2 YEARS	3 YEARS	5 YEARS
DOSE	0.125 gramme	0.25 gramme	0.375 gramme	0.5 gramme

The dosage should be relatively rather larger for children than for adults, and it was at first recommended that foods containing sulphur should be avoided, though it may be that it is more important to avoid alimentary disturbance by purgation than to eliminate foods containing sulphur. More recently the validity of the objection to the administration of sulphur has been contested. In meningitis it is inadvisable to force fluids upon the patient, as this would cause a rapid elimination of the drug and lower its concentration in the blood, but there is no reason for restricting fluid. If sulphathiazole (M & B 760) is given in the hope of overcoming a staphylococcal infection fluids should be given freely, as there appears to be a slight risk of the deposition of crystals in the kidney and subsequent formation of calculi. The dosage of this drug should be 50 per cent greater than that of prontosil or sulphapyridine. There is not any advantage in intravenous administration unless the patient is unable to swallow, or the drug causes vomiting when given by the mouth. Besides vomiting, headache, giddiness, and malaise are common toxic effects and drug rashes have been observed. It is suggested that vomiting is sometimes due to the irritation caused by hard particles of the drug prescribed in tablets. This can be avoided by prescribing the drug in the form of cream made with tragacanth; a tablespoonful of the cream corresponds to one gramme of the drug. Cyanosis is not regarded as having any significance, but it may be treated by the administration of methylene blue, 0.2 gramme by the mouth. An occasional blood count is advisable lest a leucopenia or the rare but dreaded agranulocytosis should supervene.

In the treatment of inflammation of the paranasal sinuses the same rules for diagnosis and precautions in administration should be observed as in the treatment of acute suppurative otitis media and its complications; local treatment with suitable astringents and lavage when required should not be neglected. Attempts have been made to treat chronic sinusitis by chemotherapy, but as elsewhere it is in the acute infections that satisfactory results are obtained.

Acute tonsillitis

It is now usual to treat acute tonsillitis by chemotherapy, and it is generally believed to shorten the course materially, but it is difficult to assess with any precision the effect upon a disease which ordinarily undergoes spontaneous cure in a short time. Prontosil should certainly not be given in any case in which there is reason to suspect that a quinsy is forming. This can be treated only by evacuation of the pus, and the effect of the drug may be to mask the condition and prolong the illness. It is doubtful therefore if in simple tonsillitis prontosil should be used at all, but in the acute septic pharyngitis which F. Semon described in 1895, a grave disease of streptococcal origin associated with a swinging temperature and usually with albuminuria, and having a close relationship to erysipelas, the use of sulphanilamide may save the life of the patient. As such patients have severe dysphagia intravenous administration in glucose saline may be indicated.

Infections of mouth and pharynx

The streptococcal infections of the mouth and pharynx have always been a menace after major operations on the pharynx and larynx. In these operations the planes of the neck are exposed to direct infection from the mucus of the pharynx, so that sloughing is frequent and sometimes septicaemia follows. W. Trotter drew attention to this in his Hunterian lectures in 1913, and showed how the danger can be minimized by preliminary extraction of the teeth. Laryngectomy sometimes failed in the past because the patient drifted into a subacute septicaemia to which he ultimately succumbed. Attention to technique, particularly to haemostasis and to suture of the wound so that no raw surface is left exposed to pharyngeal mucus, does much to overcome the

danger, but it is always present, especially in patients who have long been edentulous and have lost the immunity which results from recent extraction. Several cases of laryngectomy have now been rescued from an overwhelming septicaemia by the administration of prontosil. A striking instance of this kind of pharyngeal infection is that of a young man whose lower pharynx was perforated one evening by a duck bone impacted transversely across it at the junction with the oesophagus. The following morning he was gravely ill with swelling of the neck. Incision showed that the muscles at the root of the neck were already becoming gangrenous. Although there was severe sloughing and leakage from the cervical oesophagus for several days this patient made a complete recovery by the aid of prontosil administered intravenously.

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INFECTIONS, ACUTE

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EPIDEMIOLOGICAL TRENDS IN WAR

It is inevitable that a review of the acute infectious diseases in war-time should include a comparison with epidemiological events in previous wars, especially the war of 1914-18; there is still time to profit from its lessons for future guidance as the war proceeds on its course. The waging of war has invariably been attended by an increase of communicable diseases, and until the Franco-Prussian war of 1870 more soldiers were lost by disease than by military action. Before that time, enteric fever, cholera, and dysentery, all ingestion infections, were the main killing diseases, but in the present century they have been kept in check by sound sanitation in both peace and war. In the war of 1914-18, apart from Russia, Poland, and certain Balkan countries, notably Serbia, where all three ingestion diseases and typhus were very prevalent, two inhalation diseases, influenza and, to a less degree, cerebro-spinal fever, caused the principal epidemics; both were wide-spread and lethal in regions remote from the war zone, no continent and hardly a country escaping their ravages. The ingestion diseases were more restricted in time and localized in place; in the French army enteric fever was prevalent in the first two years of the war but declined to a negligible amount after the introduction of compulsory inoculation; dysentery was frequent amongst the German forces especially on the eastern front, and the British troops in the Dardanelles suffered heavily from diarrhoeal disorders.

THE PRESENT WAR

The present war differs from previous wars in that the civilian population is exposed to the same hazards and hardships as soldiers and to the conditions which favour the spread of epidemic disease, namely, close aggregation of individuals for varying periods, irregular, unbalanced, and inadequate dietary, lack of sleep, fatigue often aggravated by exposure or fear, and inadequacy of facilities for personal hygiene and communal sanitation. The mass transfer of the most susceptible portion of the community to relatively unimmunized rural communities where facilities for segregation and treatment were few was calculated to aggravate rather than counteract these conditions. Especially it was considered that measles, an epidemic of which was confidently predicted in the winter of 1939-40 in accordance with the established law of biennial periodicity, would prove disastrous in these communities. On the contrary, this particular epidemic did not materialize at the expected time either in the large cities or in reception areas, although in the late spring of 1940 measles appeared and eventually attained epidemic proportions in turn in Manchester, Liverpool and the industrial towns of Lancashire and Yorkshire, and in Birmingham, while localized outbreaks occurred in certain urban and rural areas. London was not visited by the disease until the winter of 1940-41 and the epidemic did not approach the level of previous epidemics, even when allowance was made for the numbers evacuated. Not only measles but scarlet fever, diphtheria, and whooping-cough were exceptionally infrequent in the first seven months of the war (P. Stocks, 1940). A combination of factors was responsible for this happy state; a large proportion of those of susceptible age were on holiday or had not returned to school when war broke out and exposures were therefore exceptionally few at the time they were scattered under evacuation schemes; non-immune persons known to have been exposed were debarred from entering reception areas; school attendances were staggered, residents and evacuees alternating on morning and afternoon sessions. Moreover, the autumn of 1939 was particularly fine, favouring an outdoor life, and communal indoor recreations were restricted.

During this period only two trivial diseases, chicken-pox and, to a less degree, German measles, were more frequent than usual, affecting adults almost as much as children. By the middle of 1940, however, the incidence of common epidemic diseases, especially diphtheria, scarlet fever, measles, whooping-cough, and poliomyelitis, equalled or exceeded that of the corresponding period of the previous year, but in the majority of cases remained below the level of the last normal year, 1938. About this time enteric fever became fairly prevalent, approximately four times the level of 1939; although differentiation between typhoid and paratyphoid fevers was not made in the notification returns until July 1941, the low case-fatality suggested that the latter was the predominant type. During the whole of the year notifications of enteric fever numbered 2,800 as compared with 1,500 in 1939. Exact information on the incidence of influenza is not available as the disease is not notifiable, but the returns of deaths from it in the principal towns indicated an undue prevalence in the first quarter of 1940. The more or less normal age distribution of the disease, with high attack rate in the older age groups, suggested abnormal prevalence but not severity. Influenza morbidity and mortality were considerably lower in 1941; at no time was there reason to think that the appearance of a virulent type or serious epidemic similar to that of 1918 was imminent. The experience of the years 1915-16-17 when 2,566, 1,306, and 1,465 cases of cerebrospinal fever were notified, respectively, compared with just over 300 cases in the two immediately preceding years, suggested that an epidemic of this disease was highly probable; the forecast was amply confirmed by events. Although the unprecedented number of 12,000 cases was recorded in 1940, the percentage increase over the two immediately preceding years, when the number averaged 1,383, was not much greater than in 1915, and so far 1941 has closely imitated 1916 in respect of both prevalence and lowered severity. Although prevalence was higher at the beginning of 1941 than at the same period of the preceding year the rate of increase as the year advanced was considerably lower. The acme of the epidemic was reached a week earlier but was much lower, and decline was leisurely and interrupted by exacerbations due to small local outbreaks; in the first 26 weeks 7,847 cases were notified, as compared with 9,229 in the first half of 1940. But the most striking difference from the 1915-17 epidemics has been the fall in case-mortality from approximately 65 per cent to an average of 10 per cent and in some districts to as low as 5 per cent. In a series of hospital cases the last mentioned figure has been more than halved (H. S. Banks, 1941).

Conclusions

In brief, the war so far has brought to light only three diseases in epidemic form, cerebrospinal fever, influenza, and German measles, and an abnormally high prevalence of enteric fever, bacillary dysentery (almost entirely Sonne type), and chicken-pox; in every instance case-mortality has remained low. The incidence of diphtheria, scarlet fever, measles, and whooping-cough has generally been below pre-war levels, but localized outbreaks of severe diphtheria in some centres have given cause for anxiety and have led to renewed campaigns for mass immunization.

RECENT ADVANCES IN CONTROL

Enteric fevers

Diagnosis

The H and O antigens in the Widal test continue to assist in the differentiation between the inoculated and the attacked, but the inclusion of vi-antigen has not completely fulfilled early expectations, though it is of value in the detection of carriers. Recently a classification of *B. typhosus* strains based on bacteriophage activity has been introduced; this is an important development and may well prove of great value in tracing the source of outbreaks (J. Craigie and C. H. Yen, 1938).

Treatment

Though the hopes raised by promising reports of vi-antigen antiserum have hardly been justified by subsequent experience, further refinements in the

technique of preparation may well yield better results. Despite the theoretical objections to sulphonamides on account of the tendency of both disease and drug to produce leucopenia, small series of cases have been treated by these drugs; usually the dosage employed was inadequate and the therapeutic action far from clean-cut. From a recent experience T. L. Hughes and H. F. Harwood (1940) considered that the period of infectivity was shortened but they were unable to record any effect on the course of the disease.

Prophylaxis

Active immunization of individuals living in bombed cities is desirable in view of risk of damage to adjacent water mains and sewage disposal systems. Ordinary T.A.B. vaccine is still preferred in the United Kingdom to detoxified, alum-precipitated, or endotoxoid preparations, as giving more solid and durable immunity. A. Felix recently (1941) stated that ordinary vaccine killed by heat and preserved in phenol stimulates only small amounts of vi-antibody, whereas alcohol-killed vaccine induces it in full protecting power in nearly 50 per cent of humans after subcutaneous inoculation. It has been found both convenient and effective to combine T.A.B. vaccine with tetanus toxoid (I. H. MacLean and L. B. Holt, 1940). Two injections are given at an interval of 4 weeks as tabulated below:

	(a)	(b)
<i>B. typhosus</i>	500 million organisms	1,000 million organisms
<i>B. paratyphosus</i> A	250 " "	500 " "
" B	" "	" "
Tetanus toxoid	0.9 cubic centimetre	0.9 cubic centimetre

It was found that the reactions resulting from the combined prophylactic were not greater than those which supervened on administration of the antigens singly; the immunizing effect of 2 doses of T.A.B. vaccine was at least equal to that conferred by using the customary weekly interval, whereas the tetanus antitoxic titre was more than 5 times greater than is usually obtained if the antigen were injected alone.

Dysentery

Diagnosis

The occurrence of diarrhoea in a number of subjects in a community should suggest the presence of dysentery (commonly the Sonne type in the United Kingdom) or food poisoning (*salmonella* and *S. aureus*) as well as enteric fever; the symptomatology in mild cases may be indistinguishable from other infections, since mucus, blood, and tenesmus are often absent, especially in the young. In the majority of cases the dysentery bacillus is readily isolated from the faeces and rectal swabs; the latter give a higher percentage of positives if immediate inoculation on a culture medium is possible (R. Cruickshank and R. Swyer, 1940). If not, some glycerin-saline or broth at the bottom of the swab-tube may serve to keep the organism alive. Although strains differ considerably, the organism is admittedly more resistant to the usual agencies than are the majority of intestinal pathogens. Much better cultural results than are possible with MacConkey's medium are obtainable with desoxycholate-citrate agar medium (E. Leifson, 1935; B. R. Pestana and M. J. Faraco, 1940) and its recent modifications, and the presence or absence of xylose-fermentation may be used to identify the infecting organism and to detect the source of infection in localized outbreaks, which commonly involve nurseries, residential schools, and mental institutions. A retrospective diagnosis may be made in cases from which cultures have proved to be negative—either because they were missed or examinations were made only after the bacteria were eliminated—by agglutinating a standard suspension of smooth organisms with the patient's serum. Cruickshank and Swyer obtained positive results in nearly three-fifths of their cases; agglutination usually appeared early and increased in degree as convalescence was established, but neither age nor severity of the disease appeared to have any influence on the frequency of positives. The test is of particular value in young children in whom a positive response is rare in the absence of clinical attack.

Treatment

Although favourable results have been recorded with the sulphonamide drugs, caution is particularly needed in forming an opinion on their therapeutic action in view of the mildness of the disease (G. J. Bell, 1941). In America, where Flexner dysentery is perhaps as common as the Sonne form, sulphanilylguanidine has been used with encouraging results (E. K. Marshall, Jun., A. C. Bratton, Lydia Edwards, and Ethel Walker, 1941). As the drug is poorly absorbed, it is possible to give large doses, 3 grammes three times a day for 10–14 days, without risk of intolerance. Personal experience with the substance in Sonne dysentery in Great Britain has yielded variable results; apparent success in rapid elimination of the organisms from several acute cases and carriers has been offset by a number of failures; these anomalies may be expected until the conditions governing its action as an intestinal disinfectant are better understood. (See also p. 100.)

Cerebrospinal fever

The most striking features of cerebrospinal fever in the present war have been (a) the marked reduction in case fatality and (b) the comparative frequency of meningococcal septicaemia.

Diagnosis

When the infection has become localized in the meninges, clinical diagnosis is fairly obvious and may readily be confirmed by spinal puncture, but abortive or septicaemic attacks may be overlooked. The occurrence of irregular fever with or without cutaneous manifestations should suggest the need for cultivating the blood and testing for complement-fixing bodies. In a recent small series of cases in which influenza, rheumatic fever, erythema nodosum, and trench fever were imitated, bouts of fever were accompanied by shivering or rigors, migratory joint pains and crops of macules, petechiae or nodules ('blind boils'); rapid cure was obtained by sulphapyridine (A. W. Stott and W. S. C. Copeman, 1940). As positive blood cultures were obtained in 3 only of the 17 cases the therapeutic response was with doubtful justification regarded as confirmatory of the diagnosis. R. Cruickshank has recently shown (1941) that the complement-fixation reaction is present as early as the second week or even earlier in meningococcal septicaemia, which is commonly termed 'chronic', but all gradations of severity and duration may be encountered. Further investigations (personal communication) have revealed that Group 2 strains are almost as common in septicaemia as the more virulent Group 1 organisms usual in established meningitis. The frequency of Group 2 organisms in septicaemia suggests that individual resistance may be responsible rather than feeble pathogenicity of the invading organism.

Treatment

Although a few workers at the onset, and especially for fulminating cases, still combine immune serum, usually given intravenously, with sulphonamides, the majority rely entirely upon the latter, aiming at a rapid concentration of 5–6 milligrams or more free drug per 100 cubic centimetres in the cerebrospinal fluid. The untoward effects of both oral and parenteral administration of sulphapyridine have led to a preference for the less toxic preparation sulphathiazole, although not all workers are agreed that it is equally effective. In Banks's hands both compounds have given the remarkable low case-mortality of 2.1 per cent in 96 consecutive cases treated in 1940. Spinal drainage is generally unnecessary but occasionally it is required to relieve pressure symptoms such as headache, restlessness, or slow pulse and respiration rates.

Prophylaxis

As the bacteria may be rapidly eliminated from carriers by a course of sulphapyridine it is logical to conclude that infection after intimate exposure may be prevented by similar means. R. W. Fairbrother (1940) was able to conclude from his investigations on cases treated intensively with sulphapyridine for another condition that the drug warded off infection by the meningococcus; he also found that established carriers cleared up rapidly under the drug but doubted

if swabbing to detect carriers was justified except in closed communities or in cases which originated from an identified source. In view of the probability of frequent re-exposure during epidemics and the impracticability of maintaining an adequate concentration of sulphonamide in the blood over prolonged periods, local application of powder may serve instead, but it does not appear to have been tried on an adequate scale. Mass prophylactic inoculation with meningococcus vaccine has not been regarded as worth while in Great Britain but might be applicable if large-scale epidemics occurred. The method was used in Cyprus apparently with some measure of success, but the difficulty of conducting proper control observations was a serious disadvantage in evaluating the results (I. H. MacLean and C. E. Bevan, 1939).

Diphtheria

Diagnosis

The majority of investigators of the method have reported unfavourably on Mansulo's rapid technique in which potassium tellurite solution is used (Hester Woodcock, 1939; J. F. Murray, 1939). Growth on Loeffler medium and plating on tellurite with or without direct implantation on tellurite, followed by sugar fermentation, are the standard bacteriological procedures. With experience the different types can be recognized with confidence and only 'mitis' strains require to be subjected to virulence test on the guinea-pig. The majority of workers regard direct smear examinations, especially with negative findings, as being too unreliable for routine work.

Treatment

Frequent disappointments with commercial antitoxins produced from the standard P.W. strain toxin, especially in the hypertoxic attacks associated with 'gravis' and some 'intermedius' infections, have increasingly directed attention to the need for more specific therapy. In the course of recent investigations on the constitution of diphtherial toxin R. A. Q. O'Meara (1941) claimed to have identified two components which he named substances A and B respectively; he further stated that commercial antitoxin contains a sufficiency of antibody to the former but a deficiency to the latter, in consequence of which it is rendered non-avid in the body and allows substance A to exert its lethal effects. Preliminary clinical trials with the new avid serum were dramatically favourable as shown by rapid subsidence of toxæmia and disappearance of membrane and the remarkably low case-mortality of 6.2 per cent amongst 16 cases selected for their severity, compared with the exceptionally high figure of 40.0 per cent amongst 20 unselected consecutive cases treated by control serum (C. J. McSweeney, 1941). Larger trials with this serum will be needed to establish whether or not the new conception of the nature of diphtherial toxin and its neutralization is accurate. Meantime adjuvants continue to be used in treatment. Adrenal cortex preparations, eucortone cortiron, per-corten or syncortyl (desoxycorticosterone acetate) are used by many on the assumption that toxæmia is directly dependent upon the amount of adrenal damage, which may be roughly assessed in life by the degree of alteration of the normal sodium-potassium ratio of the blood. Clinicians find it difficult to advance proof that these preparations have a positive action in correcting the disordered metabolic processes in diphtherial toxæmia. The hopes that treatment with concentrates of vitamin B₁ would prevent or cure diphtheritic polyneuritis have not been fulfilled; in the latest study, the authors were unable to discover any prophylactic or therapeutic effect (G. E. Donovan and M. Bannister, 1941).

Prophylaxis

There is still considerable diversity of practice as regards choice of prophylactic, dosage and spacing of injections. Obvious desiderata are (a) efficiency, (b) absence of reactions, (c) reduction of injections, and (d) rapidity of immunization. For children under 8 years of age there is little difference between alum precipitated toxoid (A.P.T.) and diphtheria toxoid or anatoxin (F.T.), but as only two injections of the former are needed as compared with three of the latter, it would appear to be the reagent of choice. J. T. Lewis (1941) states

that it is used in some 40 per cent of the immunization schemes investigated in Great Britain and urges its general adoption. For older subjects, especially those giving pseudo-positive Schick reactions, the blander diphtheria toxoid-antitoxin floccules (T.A.F.) preparation (3 injections) is often preferred. In schedules of mass immunization the preliminary Schick test is usually dispensed with; though this is probably permissible in children of pre-school age in the absence of a history of clinical attack, omission of a post-immunization test is never justifiable; sooner or later the penalty is disaster for the individual and disrepute for the measure. No progress has been made in this country in regard to the use of Jensen's method of nasal instillation of diphtheria antigen to confer active immunization. The latest reports of its employment have shown that only moderate success attends this form of prophylaxis (I. Kodama, S. Sato, and M. Hata, 1940).

The use of insufflations of antiseptics on the nasal mucosa in the endeavour to eliminate organisms was raised again by M. E. Delafield, Edith Straker, and W. W. C. Topley (1941), using proflavine, penicillin, and sulphathiazole for their investigations. Success with the method was reported in a diphtheria carrier, but personal experience of the measure in large numbers of contact and convalescent diphtheria carriers has suggested that it has only a limited application, and recrudescence of the carrier state is prone to occur if subjects are re-exposed to infection (A. M. M. Payne and Gladys Auchinleck, 1941).

Scarlet fever

Diagnosis

The extreme variability of scarlet fever, ranging from a transient afebrile erythema to a heavy eruption with prostration and septic complications, not infrequently renders diagnosis difficult without the aid of bacteriological and serological tests. Tonsillitis without rash, even though caused by a fully toxigenic Group A strain of *Streptococcus pyogenes* and capable of producing scarlet fever on transmission to non-immune persons, cannot properly be regarded as scarlet fever. Any of Griffiths's common serological types, 1, 2, 3, 4, 6, 8, or 12, may be feebly or even a-toxigenic and therefore, temporarily at least, incapable of causing scarlet fever; it is assumed, though without adequate proof, that repeated passages through human beings restore or enhance toxigenicity.

Treatment

Scarlet fever antitoxin to neutralize the initial toxæmia in all but the mildest attacks, and sulphanilamide to combat the invasive properties of *S. pyogenes*, are now universally used, the only difference in practice relating to the choice of antitoxin; in Great Britain immune serum from horses is commonly employed, but some American workers prefer convalescent serum on the grounds that it contains specific antibodies other than antitoxin to which they attribute its superior action (W. Thalheimer, 1940).

Prophylaxis

The ubiquity and the ease with which the streptococcus may secure a footing on the mucosa of the upper respiratory tract even of those immune to scarlet fever make prophylaxis difficult. In winter months when catarrhal affections are prevalent the streptococcus carrier rate rises steeply, especially in overcrowded communities. Attempts have recently been made to limit the spread of atmospheric pollution in hospital wards by ultra-violet radiation (L. H. Barenberg, D. Greene, and L. Greenspan, 1940), by antiseptics in the form of a fine mist, termed aerosols (R. Cruickshank and C. Muir, 1940), and by bactericidal smokes, such as incense (C. C. Twort and A. H. Baker, 1940), and J. C. Thomas and M. Van den Ende (1941) have sought to prevent the dust from rising to pollute the air by application of crude liquid paraffin (spindle oil) to floors and blankets. Avoidance of reinfection in fever hospital wards would undoubtedly lower relapses and complications and permit earlier release from isolation with diminished risk of causing 'return' cases. These problems continue to be tackled from different points in both the laboratory and the field.

Measles*Diagnosis*

Insufficient use has been made of the blood changes in arriving at a diagnosis in doubtful cases of measles, especially those without Koplik's spots (about 10 per cent). The recent work of M. Hynes (1940) has shown that whereas measles and German measles can be readily distinguished from scarlet fever and glandular fever, they cannot be distinguished from each other. In German measles the onset leucopenia is characterized by absolute lymphopenia in all and absolute neutropenia in one-half of the cases; the former is gradually converted to lymphocytosis after the fifth day and the latter to neutrophil leucocytosis after the tenth day. Turck cells were invariably present and reached their maximum about the fourth day, and plasma cells were found in one-half to two-thirds of the cases in the first week but thereafter disappeared. In measles Hynes found slight differences from the above, but the disturbing effects of septic complications altered the leucocyte picture and rendered differentiation of the two diseases impossible (personal communication).

Treatment

No new developments in treatment have been recorded since the use of the sulphonamides has become general in the prevention and cure of septic complications.

Prophylaxis

(a) Passive. Convalescent serum has remained the most efficient prophylactic, but difficulty in securing adequate supplies is a serious obstacle to its general employment. Adult serum, on the other hand, is available in large amounts, especially from 'pooled' blood banks, either fresh or dried; efforts to enhance the antibody content by taking out the globulin fraction, as is done in respect of placental extracts, have not been sufficiently successful to make it a routine preparation. Recent Canadian experiments on late convalescent serum, collected 5 to 22 months after attack, concentrated to half its volume by a cellophane bag method have given promising results but do not compare in efficacy with recent convalescent serum (Thalhimer).

(b) Active. Endeavours to confer active immunity against measles are not new, but a necessary preliminary to the method becoming a practical proposition is the identification and isolation of the causal organism. In the course of recent work G. Rake and M. F. Shaffer (1940) claim to have cultivated the measles virus on the chorio-allantoic membranes of chick embryos with which they inoculated young monkeys and produced a disease similar to that described in these animals by previous workers, and thus rendered them immune to subsequent inoculation of material from human cases. Subsequent to these observations J. Stokes, Jun., and G. Rake (1940) inoculated presumed non-immunes by nasal instillation or subcutaneous injection with virus attenuated by repeated egg passages and claimed to have rendered them insusceptible to measles. Although the human observations have been on too small a scale to meet the criticism that antecedent immunity (in the absence of a test to denote susceptibility) may have been the explanation of their apparent successes, there are grounds for the belief that further advances in measles prophylaxis and control will be along these lines.

Whooping-cough*Diagnosis*

The cough plate technique using the enriched Bordet culture medium remains the best single diagnostic method, but in the early stage, and in infants at any stage, there may be difficulty in obtaining satisfactory inoculation of the plate; in these cases a laryngeal or nasopharyngeal swab may be usefully substituted. In doubtful or abortive attacks leucocyte counts and complement-fixation tests are of value but skin tests give too inconsistent results to merit reliance.

Treatment

Adequate dietary with sufficiency of vitamins, especially ascorbic acid, sulphapyridine in the prophylaxis and treatment of complications, such as broncho-pneumonia and otitis media, and phenobarbitone to control unduly

violent paroxysms remain the chief measures. Vaccines are rarely of value except possibly in the early stages of attack and are positively contra-indicated in the presence of pneumonia or severe bronchitis. Its uncertain therapeutic action and the difficulty of securing supplies alike forbid wide use of convalescent serum. The latter objection may be overcome to some extent by the employment in its stead of immune serum from donors actively immunized with pertussis vaccines (A. C. McGuinness, W. L. Bradford, and J. G. Armstrong, 1940).

Prophylaxis

It is generally agreed that a straight vaccine prepared from phase 1 organisms grown on Bordet medium is superior to detoxified or undenatured vaccines (Charlotte Singer-Brooks, 1940). Increasing doses, 5-6 in number and depending on the reactions provoked, at intervals of 5-7 days, making a total of some 80,000 million organisms, are commonly employed, but MacLean (1940) recently urged the use of a smaller dosage—3 injections each of 4,000 million organisms at intervals of 3-7 days and a final injection after an interval of a month. In subjects recently exposed an initial small dose may be regarded as a wise precaution as reactions in these are occasionally severe. The immunity response may be estimated with fair accuracy by determining the amount of complement-fixing bodies in the blood. Attacks in vaccinated children are infrequent and mild and would probably be abolished altogether if immunity were reinforced by an injection at 2-3 yearly intervals or whenever whooping-cough is prevalent.

EPITOME

Even in war-time the chances and dangers of communicable diseases would be greatly reduced if the knowledge in our possession, imperfect as it is, were exploited to its logical conclusion. The youngest being most vulnerable should benefit first.

Immunization Scheme (after D. T. Fraser (1939), modified)

AGE	REAGENT	METHOD	NOTES
3-6 months	Vaccinia calf lymph	Single insertion linear scratch or incision $\frac{1}{8}$ - $\frac{1}{4}$ in.	Elementary bodies suspension and intracutaneous inoculation unreliable. Test: re-vaccination (if no take)
6-9 "	Pertussis vaccine, phase 1 organisms	5 graduated doses subcutaneously. 5-7 days intervals	Dosage according to reactions. Test: complement-fixation
9-12 "	Diphtheria antigen A.P.T. or F.T.	2 or 3 doses intramuscularly. 3 weeks intervals	Test: Schick or titration of blood antitoxin
18 "	Pertussis vaccine, reinforcing dose	1 injection	Test: complement-fixation
1-2 years	Scarlet fever toxin	4 or 5 increasing doses according to tolerance, intramuscularly	Scarlatinoid syndrome occasionally. Test: Dick
2-4 "	Diphtheria antigen reinforcing dose	1 injection	Test: Schick or titration of blood antitoxin
5-10 "	Vaccinia calf lymph, reinforcing	Linear insertion	

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LUNG AND PLEURA DISEASES

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During the past two and a half years experience has been gained in the treatment of thoracic injuries on modern lines, and some conclusions may be drawn and comparisons made with similar conditions treated in the war of 1914-18.

THORACIC INJURY

Patients with thoracic injury may be divided into three classes: (1) those who die immediately from severe damage to the heart, great vessels, lungs, or thoracic cage; (2) those with derangement of the mechanics of the chest, which increases the gravity of shock and haemorrhage; (3) those who survive the immediate injury but in whom infection subsequently develops in the chest, resulting in severe and prolonged morbidity, and in a considerable late mortality from sepsis and its complications.

Importance of early surgery

When the medical history of the present war comes to be written, the provision of a freely available supply of blood or its derivatives will probably rank as the most important single advance in treatment as compared with the war of 1914-18. The early administration of sufficient blood or plasma makes surgical intervention possible, within the first few hours before infection becomes established, and in patients who otherwise would be deemed moribund. The art of the anaesthetist and the simplified administration of a high concentration of oxygen by the B.L.B. mask are other important factors in making possible early surgery with primary healing. The value of early surgical intervention in chest wounds was well illustrated by a comparison of a series of air-raid casualties, treated within a few hours, with a series of casualties of the B.E.F. evacuated from Dunkirk and wounded 2 to 7 days previously. In the first group, even although many of the patients were elderly and of poor physique, wounds healed by first intention, and mortality and morbidity were negligible, the majority being discharged from hospital in 3 to 5 weeks. The casualties from France consisted of men who had survived the battle-field and the journey to England; tissues were secondarily infected, with consequent complications, such as secondary haemorrhage, empyema, massive collapse of the lung, and other conditions. Although the mortality was low, many of the severely wounded having died on the battle-field, the morbidity was high, patients remaining in hospital for many months and permanent impairment of function being common.

Special chest units

B. E. Linberg (1940) reports on 972 Russian chest casualties in the Russo-Finnish war, dealt with in a special chest unit at the base, and with a mortality of only 3 per cent; of these about half had severe wounds elsewhere. He attributes this remarkably low death-rate to (1) a properly organized chest unit, to which casualties were brought early, 65 per cent by air; (2) the excellent physique and health of the men; (3) the frequency of bullet as opposed to shrapnel wounds; and (4) the early removal of blood in haemothorax. There is strong evidence in favour of specially equipped units for chest injuries. Apart from the special experience required of the surgeon, anaesthetist, and resident medical officers, the nursing staff require training in the recognition of the sudden complications which are common (spontaneous pneumothorax, air-embolism, sucking wounds, cardiac tamponade, and the like), in the supervision of 'closed drainage' tubes, and in the use of oxygen. In each case frequent radiography by a portable plant is essential. There should be a staff

of masseuses with experience of the various types of remedial exercises for different chest conditions.

Treatment of chest casualties

There is little doubt that there is still too much delay in patients with chest wounds being seen by the surgical specialist, and it must be insisted that early surgical treatment may be required quite as much in chest cases as in those of injury of other parts of the body. Treatment of shock should be started at once by the usual methods, and with oxygen by the B.L.B. mask, and by transfusion if indicated. Only first-aid measures to save life should be taken during this period, namely (1) sucking wounds should be closed by a large pad of vaseline gauze strapped to the chest wall; (2) tension pneumothorax should be relieved by introducing into the pleural cavity a large hypodermic needle connected by rubber tubing to an under-water seal on the floor; (3) crushed ribs or 'stove-in' chest should be treated by firm strapping round the lower chest, putting the patient in a comfortable sitting-up position, and administering oxygen with a B.L.B. mask. As the patient may be unable to cough up the blood or mucus which collects, aspiration through an intra-tracheal tube may be necessary. A skilled opinion should be obtained as soon as possible after the patient has recovered from the initial shock, but a 'penetrated' radiograph in the antero-posterior and lateral positions is of the utmost value, and every effort should be made to have this done first. The surgeon then decides on clinical and radiological evidence as to the type of injury, and whether surgical treatment is required.

Indications for primary operation

C. P. Thomas (1940) gave the following indications for primary operation within the first 6 hours: (1) open sucking wounds; (2) haemothorax which is overt and progressing; (3) haemothorax, when there is reason to suppose that other structures than the lung have been injured, such as the pericardium or diaphragm; (4) haemothorax with retained foreign body; (5) haemothorax with massive clot in the pleural cavity. Primary operation consists of 'surgical revision' of the entrance and exit wounds, thoracotomy, removal of foreign bodies, and resection of damaged lung. The pleural cavity is usually drained through a separate stab wound for 48 hours by 'closed drainage'.

Contra-indications to operation

The contra-indications to operation in the first few hours are (1) through and through wounds without haemothorax; (2) haemothorax with through and through wounds which do not constitute sucking wounds.

Retained foreign bodies

Patients who have recovered from the immediate effects of injury, but who have a retained foreign body in the lung or pleura, require consideration. J. E. H. Roberts (1941) quotes data of 80 cases seen at the Ministry of Pensions hospital after the war of 1914-18; the patients were treated surgically, with one death only. In the majority, symptoms (haemoptysis, cough, expectoration, pain, and dyspnoea) persisted from the time of injury, but in 28 cases there was an interval of freedom from symptoms after recovery from the wound, this varying from 1 to 13 years. Obviously there must be a large number of symptom-less cases, with retained foreign body, from the war of 1914-18, but no figures are available. In the present war such cases should be constantly observed for some years to see in how many patients symptoms develop later in life. It would seem logical to advise surgical treatment in those who are left with symptoms from the time of injury, but to await further experience before recommending the removal of foreign bodies which are not causing symptoms.

Traumatic haemothorax

Haemothorax is but an incident in many cases of thoracic injury and may mask the actual condition present; after removal of the blood, radiograms may show foreign bodies, fractured ribs, and damage to lungs, diaphragm, and other viscera not previously suspected. Haemoptysis is not a constant symptom in penetrating wounds of the lung.

Classification

C. Hoyle (1940) classified traumatic haemothorax as (1) 'simple', when the blood in the pleural cavity is the most important lesion; surgery is not usually indicated; (2) 'compound', when there is an additional important injury to the chest wall, lung, or other viscera, or a retained foreign body; surgery is usually indicated in this group. Careful clinical and radiological examination should serve to separate the two groups, but often it is only after the removal of the blood that the condition is found to be 'compound'. A specimen of the fluid should always be examined as early as possible by direct smear, in addition to aerobic and anaerobic cultures, since infection occurs in about 30 per cent of cases, and organisms may be seen in the direct smears. It should be noted that a sustained pyrexia of 100°–103° F. is frequent in uninfected haemothorax for a few days, and that the presence of blood in the pleural cavity causes an outpouring of fluid, thoracoscopy revealing an acute inflammatory reaction of the pleura.

Treatment

Although in the past conservative treatment appears to have been not infrequently successful, there seem to be cogent reasons for advocating early and complete removal of the blood in all but minimal cases, for the following reasons: (1) the diagnosis of the presence of foreign bodies and of other injuries is facilitated; (2) the risk of infection of the stale blood is decreased; (3) after removal of the fluid, expansion of the lung is rapid, the period of hospital treatment occupying weeks as against the months taken up when natural absorption alone is allowed; furthermore if clotting takes place, the organization of the clot results in gross thickening of the pleura, immobility of the lung and diaphragm, and flattening of the chest wall, with permanent impairment of function. I. E. Matsyev (1940) described 88 cases of 'closed' haemothorax treated in a Russian chest unit by early aspiration, when only 2 per cent became infected, and experience in Great Britain confirms the value of early removal of blood.

The treatment of *simple uninfected haemothorax* appears to be the removal of as much fluid as possible by gas-replacement on the second or third day; aspiration of fluid and air is repeated as required at intervals of 2 days to keep the pleural cavity 'dry' and to expand the lung as soon as possible. Remedial breathing exercises should be started at the end of a week. The aim of air-replacement is to avoid further haemorrhage from the lung; if bleeding takes place after gas-replacement it occurs usually from an intercostal vessel which requires ligation. If a clot forms, it should be removed by thoracotomy, although occasionally soft clot may be dealt with by a thoracoscope.

An *infected haemothorax* is not treated by gas-replacement but by repeated aspirations through a vertical incision made down to the level of the intercostal muscles, this being kept open by a vaseline gauze pack which prevents infection of the chest wall by the needle tracks. When a localized empyema with thick pus has formed, drainage by rib-resection is required. Early drainage of an infected haemothorax by an intercostal catheter and 'closed' drainage often results in a total empyema by leakage of air into the pleural cavity, the lung taking months in the process of expansion.

BLAST INJURIES

S. Zuckerman (1940) in experiments on animals exposed to blast from explosions, states that the injury varies with the distance from the explosion, that the positive pressure of the blast acting through the chest wall is probably the effective factor, and that haemorrhagic areas in the organs, particularly the lungs, were common lesions. In clinical cases it is difficult to differentiate between other factors such as wounds and injuries, damage from falling masonry, asphyxia by inhalation of plaster dust or pressure on the chest, and inhalation of carbon monoxide or other gases.

Pathology

In cases considered to be due to the effects of blast alone, G. Hadfield and others (1941) describe multiple areas of haemorrhage into the lungs, the size

depending on the survival period. Such haemorrhages are usually at their maximum in 4 hours; they appear to be capillary in origin, not related to the bronchial tree, and occur in different parts of the lung; rib markings are seen more commonly in children; haemorrhages into the intercostal spaces are common. After 36 hours the microscopical appearances suggest the red hepatization of lobar pneumonia with a fibrin network, but the cells are chiefly mononuclears (pseudo-pneumonia). Blood may be inhaled into other parts of the lung.

Clinical picture

The clinical features of blast injury are dyspnoea, cyanosis, and tachycardia, which is rather out of proportion to the physical signs in the lungs; slight cough and haemoptysis are common. Râles suggesting pulmonary oedema may be present early, and after 24 to 48 hours signs of frank consolidation with tubular breathing may appear. The radiographical appearances vary, and scattered opacities or large hilar shadows may be seen. These opacities may clear up within a few days. In severe cases the clinical picture is that of acute pulmonary oedema, and in mild cases little but some degree of tachycardia may be found. The ear drums should always be examined in suspected cases. Severe abdominal pain and rigidity may be a feature, and J. N. O'Reilly quotes two such cases in which laparotomy was negative; in one of these a necropsy revealed extensive haemorrhage along the intercostal spaces, this probably accounting for the referred pain.

Treatment

Treatment is symptomatic, with rest, administration of oxygen, and perhaps venesection outstanding; operations or giving of anaesthetics should be avoided, unless such are essential.

C. P. G. Wakeley (1941) quotes instances of similar lesions in sailors exposed while in the sea to the effects of exploding depth charges.

FAT EMBOLISM

A. H. T. Robb-Smith (1941) has revived interest in this condition by a review of 115 accident cases in which he regarded fat embolism as a significant factor in the cause of death in 25 per cent. Zuckerman did not find evidence of it in animals exposed to blast injury, and opinion among pathologists on the incidence and importance of fat embolism is somewhat divided. That the condition does occur seems undoubted, and it may explain a train of symptoms, often ending fatally, and not generally recognized at the time.

Aetiology and pathology

Fat embolism is usually a result of trauma, particularly of bones, but it may supervene in burns, manipulation of joints, therapeutic injection of oily solutions, or as a complication of poisoning by alkalis. Necropsy shows an excess of fat in the right as compared with the left side of the heart and congestion and oedema of the lungs, in which fat may be seen with the naked eye; after adding a few drops of 2 per cent potash to a small piece of lung, fat emboli may be visible, and frozen sections may demonstrate fat in large globules in the capillaries and alveoli; a low grade pneumonic consolidation may be present. Fat emboli may be seen in the brain, causing petechiae, areas of hyperaemia, and anaemic infarcts. The choroid plexuses show capillaries blocked by fat or fibrin (Dorothy Russell, 1941). Similar changes are seen in the renal glomeruli.

Clinical picture

The clinical features of pulmonary fat embolism, provided the amount of fat is large, are similar to those of a large embolism caused by blood clot. More usually symptoms commence after a latent period of 4 to 48 hours and suggest pulmonary oedema, there being dyspnoea, pale cyanosis, and raised temperature and pulse rate; the blood pressure does not fall. Death may take place during this stage, with signs of acute heart failure, but more commonly the acute phase passes on to a condition of low grade pneumonia, which may either resolve or end fatally. The sputum is frothy at first, and

later may become blood-stained or purulent, when it may contain large extra-cellular fat globules; the latter may also be found in the urine.

In systemic fat embolism symptoms do not usually appear for 2 to 3 days, when violent delirium alternating with coma is characteristic; various lesions of the nervous system may be present in a chaotic mixture. Hyperpyrexia is frequent, as are petechial haemorrhages—a feature in diagnosis—in the skin of the chest, neck, and upper limbs. Lumbar puncture is negative; ophthalmoscopic examination may show oedema of the retina, crescentic areas of pallor with haemorrhages, and sometimes segmentation of the blood in the vessels by fat. Radiographs of the chest show opacities of various sizes, these tending to disappear rapidly.

Treatment

As regards treatment, Robb-Smith suggests that before a fracture is manipulated, a tourniquet should be applied and released slowly; immobilization of the fracture should be as complete as possible. Treatment of the established condition is as for pulmonary oedema: intravenous injection of sodium desoxycholate and other emulsifying agents of fat are on trial but may in fact be harmful.

COMPLICATIONS OF THORACIC INJURIES

It does not come within the scope of this review to discuss complications, but these are common, often sudden, frequently serious, and may easily be overlooked unless close observation is maintained. Four conditions may be mentioned owing to difficulty in diagnosis: (1) acute dilatation of the stomach, especially in severe debility from prolonged sepsis; being unexpected, this is easily overlooked; (2) acute pericarditis; in association with intrathoracic sepsis it has been noted that pericardial friction may be heard for a few days without clinical or radiological evidence of fluid in the pericardial sac; in such cases, an unsuspected pleural pocket of pus should be looked for and drained if found; (3) empyema on the sound side; this may occur some time after the damaged hemi-thorax has appeared to be progressing favourably; attention may be focused wrongly on the injured side; (4) referred abdominal pain; with injury to the lower chest and diaphragm and in blast cases, severe abdominal pain is occasionally observed, simulating acute peritonitis; the point should be remembered before a laparotomy is performed.

TREATMENT OF CHEST INJURIES

Remedial breathing exercises to assist expansion of the lung and to regain full movement of the diaphragm and chest wall, together with exercises to correct deformities of the spine and thorax, are of the greatest practical value. Masseuses with special experience and considerable patience and 'drive' are required, and they can do a good deal to help the patient from the mental as well as the physical point of view. It seems important to have the patients 'up and about' as soon as possible, as this activity encourages lung movement.

Sulphonamides have proved their value in both prophylaxis and treatment of infection, but their indiscriminate use may be harmful in masking symptoms and signs, for example of retained pus. Experience goes to show that it is best to prescribe them after diagnosis is made and to remember that they are toxic as well as potent drugs. The importance of a full and varied diet, rich in proteins and vitamin C, is put on a scientific foundation by A. O. Whipple (1940) in an investigation on the healing of wounds. The average hospital diet in war-time is insufficient, particularly in vitamin C, and it might be wise to add some ascorbic acid and possibly some iron as a routine.

MASS RADIOGRAPHY

During the past five years the technique of photographing the fluorescent screen image has advanced so much that small pulmonary lesions can now be recognized with considerable accuracy by practised observers.

Methods used

Further refinements will no doubt be made, but at the present time the

method is practical and is used in the routine examination of recruits for the Services in Canada, Australia, and Germany, and for the Royal Navy. Approximately 200 recruits per hour can be photographed, and those showing abnormal shadows may be singled out for a full-sized radiograph. P. Ellman (1941) summarized published results, which show that shadows indicative of active pulmonary tuberculosis are found in from 0.25 to 1.5 per cent of recruits; among students the figure varies from 1.5 to 5 per cent in different countries. In addition to the pulmonary lesions, various cardiovascular abnormalities may be detected.

Advantages of screen photography

Screen photography, on account of its speed and cheapness, has great potentialities; in pulmonary tuberculosis, for example, it is generally accepted that the diagnosis should be made before clinical manifestations are present, and repeated radiographical examinations seem likely to be the most practical method of detecting the early lesions. At the moment, mass radiography is unlikely to apply to clinical work so much as to research on the incidence of intrathoracic abnormalities in various sections of the community, such as those comprising young adolescents in industry, schools, and universities: it may have a place in the detection of the sputum-positive cases in older groups, which has an obvious industrial value; in country districts a mobile plant might solve the difficulty of investigating tuberculous contacts. Its value can be anticipated in the preventive medicine of the future, when from early childhood to adult life a radiographical record may well be a routine part of the annual medical examination.

ACUTE PUTRID LUNG ABSCESS

Since H. Neuhof and A. S. W. Touroff (1938) published the results of early surgical drainage in 45 consecutive cases with 43 patients 'cured', and 2 with a fatal termination, the condition has received considerable attention. Papers by H. Neuhof and A. S. W. Touroff (1940), M. B. Rosenblatt (1940), and C. L. Jackson and A. R. Judd (1940) give valuable information, both as regards the late results of conservative and surgical treatment in the past decade, and as regards recent advances in surgical technique. From these observations and from the experience of workers in this and other countries, there seems to be good reason to regard acute putrid lung abscess as a clinical entity, with a serious mortality and liability to severe morbidity and sequelae.

Aetiology

In a small proportion of cases the condition follows operations on the nasopharynx or the inhalation of foreign bodies, but in the majority no clear-cut cause is found; there is good evidence to suspect the inhalation of septic material from the mouth, particularly dental tartar. The infection is anaerobic and results in an acute spreading necrosis of the pulmonary tissues, appearing at first as a patch of 'pneumonitis', but cavitation usually takes place within 14 days.

Clinical picture

The abscess invariably points towards the periphery of the lobe (and most commonly towards the parietal surface), but it may point into the interlobar fissure, the mediastinal or diaphragmatic surface. The right lung appears to be affected nearly twice as often as the left, but the incidence in the upper or lower lobes is about equal. Although the abscess may discharge into the bronchus with resultant clinical improvement, it is common for chronic suppurative changes and bronchiectasis to occur, which may prove fatal ultimately. 'Follow-up' investigations suggest that although many cases may show clinical improvement, bronchographic studies reveal gross damage to the bronchi and lung in a considerable proportion. If the term 'cured' is confined to those without any bronchographic evidence of disease, the percentage treated by non-surgical methods is small.

With accurate radiographic (and possibly bronchoscopic) localization of the abscess, H. Neuhof and A. S. W. Touroff (1940) claim that adhesions

are present, whereby a one-stage operation can be performed. This does not consist merely of inserting a drainage tube, but in removing the roof of the abscess cavity and loose sloughs of lung, and packing open the whole area, allowing free access of air while healing takes place from the bottom. In 86 cases these writers claim 73 classified as 'cured', with but 3 deaths. In view of these results there seem to be grounds for advocating surgical treatment soon after the diagnosis is definitely established, usually within 3 weeks. A small number of these abscesses may rupture into the bronchus early, and so long as a fluid level does not persist in the radiogram, such cases may do well by conservative treatment. Early bronchoscopy is probably indicated in the majority of cases to exclude a foreign body and confirm the position of the affected area of lung.

PULMONARY TUBERCULOSIS

A number of papers have been published recently on the results of cases treated by thoracoplasty operations, but the operative technique has been modified so much in recent years that it is perhaps too early to draw definite conclusions, save that the operative mortality is steadily falling and results are improving. The operation of extrapleural pneumothorax is still finding its proper level among the various measures for therapeutic collapse of the lung.

Physics and pathology of cavities

Since the paper by P. N. Coryllos and G. G. Ornstein, published in 1938 on giant tuberculous cavities, many interesting observations have been made on the physics and pathology of tuberculous cavities generally. L. Eloesser (1941) in experiments on cadavers, with bellows tied into the trachea, was able to simulate the action of coughing, and has confirmed results in the living, showing that tension or positive-pressure cavities are kept open by a valvular mechanism, whereby air distends the cavity during coughing, and by other means. Such cavities, he says, are not so likely to close by 'collapse' measures as are those non-tension cavities in which the bronchus is patent. Monaldi and others (1939) have treated successfully such tension cavities by suction drainage with a transpleural catheter into the cavity. It appears necessary in such cases to prove that the pleura is adherent by previously attempting an artificial pneumothorax in several places. H. Brunn, S. Shipman, A. Goldman, and L. Ackerman (1941) come to the same conclusions and quote instances of successful treatment of such tension cavities by open drainage and packing. These studies on pulmonary cavities are significant in affording a better understanding of pulmonary disease generally and of therapeutic procedures.

BRONCHIAL ADENOMA

This condition is becoming recognized with greater frequency owing to fuller knowledge of its occurrence and the wider application of more exact methods of diagnosis. A. Goldman and H. B. Stephens (1941) give a review of the salient features and a full bibliography. In the absence of tubercle bacilli in the sputum, recurrent haemoptysis in the second and third decades suggest the condition. When bronchial obstruction takes place, there are the added symptoms of pulmonary suppuration. The bronchoscopic appearances are described as fairly characteristic, as is the histology of typical biopsy specimens. With further experience of these tumours it appears that (1) although they may present into a bronchus, they are often of the 'collar-stud' type with a large submucous or peribronchial mass; (2) that malignant changes may take place at any time; (3) that bronchial obstruction and its consequences are likely to occur sooner or later in the majority.

Although bronchoscopic manipulations and implantation of radon may keep the patient free of symptoms for a long time, the logical treatment is surgical resection of the tumour before bronchial stenosis has developed.

CARCINOMA OF BRONCHUS

With improved technique the mortality of pneumonectomy is decreasing steadily, and an increasing number of cases of carcinoma of the bronchus are

being dealt with in this way. Further information on the late results of cases so treated is required, but as surgery offers the best hope of cure at the present time, every effort should be made towards earlier diagnosis.

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MENTAL DISEASES

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SHOCK THERAPY

The progress of treatment in psychiatry continues. The tendency in this direction is a welcome change from the traditional nihilism of the decades before the war of 1914-18. Treatment received its first real impetus from psychopathology; from the physiological side this impulse was reinforced by the introduction of therapy for general paralysis of the insane in 1917, but this was applied only to a restricted, although an important and at one time a common, mental disease. Of recent years, with the introduction of insulin therapy, but especially since the introduction of better technique in the methods of induction of convulsion therapy, therapeutic advances have been made on a wide front. The past year has seen a continuation of this advance, with a greater definition in certain sectors and a promise of new advances in other directions.

The convulsive method

At present the convulsive method occupies the front rank. Not only is it easier to carry out but it appears to have a wider range than insulin shock. A note on convulsant drugs may be useful at this point. In order to prevent any confusion which may arise from the somewhat involved nomenclature of the tetrazol convulsants it is advisable to remember that the substance originally known as cardiazol is described in the third Addendum to the *British Pharmacopoeia*, 1932, as leptazol; this has the non-proprietary synonym, metrazol, and the proprietary names, cardiazol and phrenazol. The name leptazol is used in this article although the work recorded may have been carried out with one of the proprietary brands. A triazol compound, hexazole (synonym: triazol 156), supplied under the trade name of azoman, is also used as a convulsant.

The introduction of the electrical technique makes the injection technique by leptazol and similar substances, such as picrotoxin, relatively crude. The superiority of the electrical technique lies in its simpler application, but more especially in the fact that the patient knows nothing about the actual process, or at any rate has complete and permanent amnesia for it afterwards. Moreover the fracture rate is lower, as stated by L. H. Smith and others at the 97th annual meeting of the American Psychiatric Association in 1941, and the elaborate precautions which have been suggested and used in the leptazol technique to eliminate danger of this sort are less necessary. For example, it is hardly necessary that the spine should be hyperextended or to use curare (A. E. Bennett, 1940), or β -erythroidin (S. R. Rosen and M. V. Borenstein, 1941), or quinine methochloride (A. E. Bennett and P. T. Cash, 1941) to produce local muscular paralysis and so to eliminate spasm and reduce the risk of fractures. Since the patient is amnesic afterwards the use of sodium amytal (D. W. Hastings and T. D. Rivers, 1941) or hyoscine (J. V. Edlin and E. S. Klein, 1940) or other drugs designed to minimize or abolish the period of pre-convulsive anxiety is also unnecessary.

Involuntary melancholia

The syndrome in which the convulsion method has had its most striking successes is that of involuntary melancholia, in which the results may be dramatic, as they have at any rate been in recent cases. After three or four convulsions a patient who has been deluded or hallucinated for six or nine months will rapidly lose his symptoms and become interested in the real world again. Another with profound self-destructive tendencies, ceases to be agitated and

rapidly develops insight and recovers sufficiently to be put on parole. With endogenous depressions in younger subjects the results often appear to be as satisfactory. Such conditions usually have a favourable outcome in the long run, but, as R. E. Hemphill and W. G. Walter (1941) remark, these patients may improve much more rapidly with electric shock treatment than would otherwise be expected. One drawback is that a hypomanic condition may be precipitated for a time, but the chief disadvantage is that there is not any evidence that recurrences are prevented. Results appear to be obtainable also in cases of endogenous depression with a considerable psychogenic precipitation.

Schizophrenia

The degree of success in schizophrenics is still difficult to estimate. H. O. Colomb and G. L. Wadsworth (1941) examined the results when the leptazol method was used in 97 schizophrenics and found a 50 per cent increase in the recovery rate as compared with a control group. Success was associated with certain features, the chief of which were the following: acute onset; duration less than one year; previous history of fair social adjustment; pre-psychotic personality within average limits; prominent situational factors; affective features, confusional or deliriod states; overactivity, mutism, and negativism; rapid regression. These features are indeed identical with those associated with spontaneous recovery—acute onset, psychogenic precipitation, extroversion, and pyknic physique (O. Kant, 1941). However, a sufficiently large group of controls with strictly comparable material is still lacking. The groups contrasted so far have been too heterogeneous in themselves and with regard to one another to make satisfactory conclusions possible in schizophrenia. But even if recoveries fall short of expectation, at least so far as the less recent cases are concerned it is still worth while to try the treatment in all physically fit chronic schizophrenics. Out of 37 chronic schizophrenics treated by the convulsion method Hemphill and Walter found that 2 made a complete recovery and 13 showed a degree of improvement which made them much more manageable.

Chronic anxiety states

More recently the convulsive method has been extended to chronic anxiety states of psychoneurotic form, including those resulting from war experiences, with apparently favourable results. It may be a justifiable procedure when psychotherapy has failed and when the presumption is that the aetiology of the disorder, although psychoneurotic in form, is not psychological in the sense of the presence of complexes; or when it is possible that what was originally psychogenic has become ingrained as a habit.

Fractures of vertebrae

The possibility of the occurrence of vertebral fractures caused by whatever method convulsion is induced still remains of interest, although it appears to be less common with the electric shock method because of its lesser violence, and although in fact such fractures are usually symptomless. In an examination of this question L. C. Cook and D. E. Sands (1941) found 21 out of 143, or only about half the average of other published series. They attribute this result to the avoidance of all forms of restraint. Similar fractures have been found in 10 per cent of idiopathic epileptics without any disability having ever been reported; so far delayed vertebral collapse (Kümmel's disease) has not been observed either in epilepsy or after convulsion therapy.

Electrical convulsion technique

The technique of the induction of electrical convulsions is described by Hemphill and Walter. In order to avoid the hyperflexion of neck and trunk which is thought to be responsible for vertebral fractures, they treated the patient on a hard flat couch without a pillow and without restraint to the trunk. As contra-indications to such treatment they mention pyrexia, any severe heart lesion, recent tuberculosis, any organic disease of the central nervous system, any important bodily illness, more than a slight degree of albuminuria, and a concurrent course of prophylactic vaccine inoculations. Age is not a contra-indication; not infrequently patients up to 70 have been treated successfully; Hemphill and Walter's oldest patient was 74. That the

contra-indications they suggested are justified to some extent is supported by the observation that among 320 schizophrenic patients examined twelve months after treatment (in this instance by leptazol) pulmonary tuberculosis was shown in 8 per cent (compared with 3 per cent of a control group), myocardial damage indicated by the electrocardiogram occurred in 5 cases, late epileptiform seizures occurred in 4, and 13 showed delta waves after treatment (C. F. Read and the Elgin State Hospital Staff, 1940).

The main difference between convulsions induced electrically and those produced by leptazol is in the absence of a latent period, and the wider range of duration and severity of the fits which can be obtained with the former (H. Löwenbach and R. S. Lyman, 1940).

Insulin shock

The interest in convulsion therapy, especially electrical therapy, has largely supplanted, for a time at least, the interest in the insulin shock method, mostly because of the greater ease of application, but partly because of the clinical advantages of a method which seems to have a wider range of usefulness. With acute paranoid schizophrenia, catatonia and catatonic excitements, R. Freudenberg (1941), for example, now starts with a convulsant instead of insulin and 'reserves insulin for slightly restless and anxious schizophrenics with loss in weight'. Insulin has also been extended with success to psycho-neurotic syndromes in a few cases, for example in an anxiety hysteria, and in an obsessional case (Freudenberg).

HORMONE THERAPY

It should not be supposed, however, that shock therapy, even in the group in which it is most successful—involuntional melancholias—is even now accepted as the best method by all psychiatrists. The claims of hormone therapy have been revived, partly on the ground that previously insufficient dosage was given. Thus it is claimed that theelin (oestrone) injected in oil to the extent of 30,000 to 60,000 international units produces a recovery rate of involuntional melancholias of 90 per cent (C. C. Ault, E. F. Hootor, and A. A. Werner, 1940). Some observers, such as A. Myerson, deny the validity of such results. On the other hand, 135 involuntional psychotics treated by oestrone (the dosage being assessed according to the oestrone excretion and controlled by studies of vaginal smears) showed improvement or recovery in a considerable number of patients (C. C. Burlingame and Marjorie B. Patterson, 1941). Hormone therapy has also been tried in other conditions. In impotence without discoverable organic cause testosterone propionate has been found to be no more effective than sesame oil, so that any results obtained were attributable to suggestion (H. T. Carmichael, W. J. Noonan, and A. T. Kenyon, 1941). In women the gonadal inhibiting effect of testosterone propionate has been used with temporary success in the treatment of excessive sexual urge; the good results were repeated with subsequent courses of injections in three out of four patients. One nymphomaniac complained of being desexed (H. S. Rubinstein). Of 29 overt homosexuals 25 showed male hormones relatively lower and excessive oestrogen in the urine. On the other hand, there appeared not to be any relation of a pathognomonic kind between hormone excretion and involuntional melancholia (R. Neustadt and A. Myerson, 1940).

FRONTAL LEUCOTOMY

The observation that euphoria followed injury to the frontal lobes led E. Moniz of Lisbon (1936-7) to investigate the effects of damage to the white matter of this region in certain chronic mental states. W. Freeman (1939) following his example obtained some successes, especially in chronic depressed obsessional states. Recoveries have also been claimed in cases of agitated depression, and in some hebephrenic and paranoid schizophrenias. In Freeman's series the important effect was on symptoms of the group characterized variously as anxiety, worry, nervous tension, and obsessive thinking. Recently treatment by this method has been adopted in Great Britain with some success in chronic depressions, involuntional melancholias, and schizophrenia.

Some changes in mental function of a less desirable kind have been noted, but they are not usually pronounced and are partly transitory. Emotional flattening, diminished spontaneity, facetiousness, poor judgement, perseveration, and restlessness have all been noted. One remarkable effect is change from anxiety about air raids to indifference to them. Very occasionally a severe dementia has been reported post-operatively, but on the whole in cases of very chronic anxiety or depression with obsessional thinking and in chronic schizophrenics the method appears to be worth considering (E. Lilian Hutton, G. W. T. H. Fleming, and F. E. Fox, 1941). It is true that, as has been indicated, the finer edge is taken off the personality, but it is uncommon for important deterioration to be recorded. In the types of illness indicated, in which psychotherapy and convulsion therapy and insulin shock, in that order, have failed, frontal leucotomy may very cautiously be adopted. Leucotomy is also worth consideration in schizophrenics who require what has been styled 'maintenance doses' of convulsion therapy in order to sustain their improvement, i.e. patients of this type who require a few convulsive shocks at intervals. There is a further group in which the method may prove to be worth a trial, namely in any form of recurrent mental illness in which the recurrence is sufficiently frequent to be disabling to any career of usefulness.

Technique of leucotomy

The technique, which consists chiefly in the passage of a hollow needle with a stiletto into the white matter of the frontal lobes on either side of the middle line and in section of the white matter in such a way as to interfere extensively with the frontal thalamic connexions, is described again in a paper by Hutton, Fleming, and Fox, and a modification is described by J. S. McGregor and J. R. Crumbie (1941).

TREATMENT OF SENILE TOXIC EXHAUSTION SYNDROMES

It has been found that in psychoses characterized by delirium or stupor with confusion, mainly in elderly people, the use of nicotinic acid has been attended by prompt improvement. It appears, therefore, that one type of so-called infection-exhaustion psychoses can thus be successfully managed, although the patients may not present any signs of pellagra, and apparently may not have had any dietetic deficiency. The nicotinic acid may be given either by mouth up to 600 or even 1,500 milligrams daily, or intravenously 300 milligrams daily for several weeks or until a staple result is produced. Similar successes have been claimed in delirium tremens (V. P. Sydenstricker and H. M. Cleckley, 1941).

CLINICAL EXPERIMENTAL APPLICATIONS

One effect of the newer methods of treatment described above has been to convert the patient to some extent into an experimental animal without detriment to himself or interference with treatment. Thus the relative effect of convulsant drugs and, with the aid of the electro-encephalogram, their mode of action, can be studied by administration of the drug and application of the convulsive current. In this way, for example, with sodium diphenylhydantoinate (epanutin), it has been shown that the electrical convulsive threshold is raised by the drug, which, however, is not fully effective until the sixth day after the first dose, and that some effect persists fourteen days after the last dose (Hemphill and Walter). The method of prefrontal leucotomy clearly gives an unequalled opportunity for study of the functions of the frontal lobes in human beings, since performances before and after interference with frontal lobe function can be compared in a manner not previously possible. The electro-encephalogram has also proved its usefulness in aiding the clinical differentiation between the post-traumatic psychogenic states and the psychological effects of persistent cerebral damage (D. Williams, 1941). The absence of abnormal waves, however, means simply the absence of abnormal cerebral tissue and may be due to complete destruction of damaged cerebral substance.

PSYCHIATRIC RESEARCH IN GENERAL

With such advances in the clinical field it becomes more and more necessary for the psychiatrist of the future to be not only a clinician, but to be something of a physiologist as well, and an experimental physiologist at that; or he may find it advantageous to have a training in biochemistry much beyond the average. For example, it has been shown that those with pyknic body build have high blood serum cholesterol, phospholipides and fatty acids, whereas leptosomes have low values. Schizophrenic patients tend to have low blood lipids as contrasted with manic-depressives. As in the case of muscle, so with brain tissue, it now appears that phosphorus is intimately concerned with energy exchanges in the brain (E. F. Gildea, 1941). This does not necessarily contradict the observation that the respiratory quotient of the brain is a constant approximate unity in all cases, indicating that the brain utilizes carbohydrates almost entirely (F. C. Courtice, 1940). There are increasing indications of intimate chemical relations between hormones and the brain substance (V. M. L. Golla and M. Reuss, 1941). If to this be added the observation that genetics is now becoming linked with histopathology and biochemistry, for example in amaurotic idiocy and tuberose sclerosis, it will be seen that psychiatry is about to follow physiology into a highly technical collection of special disciplines. It seems likely that the clinician will have to derive his guidance in these directions from specialists, and to concentrate as far as his own investigations are concerned on psychopathology and sociology, the latter study being one to which the war with its various dislocations is giving a considerable impetus, and on which the peace, when it comes, will confer still greater importance.

PSYCHOPATHOLOGY AND PSYCHOTHERAPY

A survey of the technique of practising psychoanalysts led E. Glover and Marjorie Brierley (1940) to the surprising conclusion that the results obtained by different analysts with different degrees of experience using somewhat different techniques, and presumably of differing abilities, are similar. This is one of those statistical conclusions which are not borne out by acquaintance with individual cases. Some psychotherapists are conspicuously more successful than others in the quality of their results. There have not been any striking modifications of general principles or important discoveries in this field recently, but certain syndromes have been further illuminated psychopathologically. For example, S. Lorand (1941) has worked on the comparatively neglected problem of the psychopathology of anorexia nervosa, and concludes that in the child's faulty relations to the mother, and in a concomitant immaturity of the ego, lies the central psychological problem in this condition. Although this may be true of some patients, the majority make a satisfactory symptomatic recovery without the use of this hypothesis; in some, however, the recovery from anorexia nervosa occurs in a neurotic personality or is followed by the appearance of neurotic symptoms of another kind. The peculiar menstrual disorder of this condition is not yet explained by any method. It is possible that it is one of those conditions in which the habitual psychophysical dualism of clinicians is a handicap to understanding. In a study of fugue states, which he interprets as episodes of compulsive wandering, E. Stengel (1941) found a tendency to pronounced changes of mood in the great majority suggesting a manic-depressive basis, and in ten cases he found evidence of an epileptic disposition. From the psychodynamic point of view the chief interest of his study lies in the observation that most of them in their childhood had had faulty relations with their parents. Fugues seemed to represent a search for something that had been missed—presumably the lost parent. Stengel draws attention to the influence of the break-up of homes by the war in facilitating the appearance of such states later. This study is an interesting corollary to the investigations of truancy in childhood carried out by Partridge some years ago, when the truancy homeward from school was shown to depend in some instances on the child's compulsive desire to

reassure himself about the safety of a parent towards whom unconscious aggressive wishes had existed.

CLINICAL APPLICATIONS OF BIOCHEMISTRY

G. Gjessing's work on the relationship of changes in nitrogen balance in periodic catatonics was alluded to in last year's Critical Survey. S. W. Hardwick and A. B. Stokes (1941) have sought to confirm his findings. From their work it appears that the evidence is against the simplest view that nitrogen change is secondary to a mental disturbance, and also against the converse view that the alterations in nitrogen content are the cause of the mental changes. The relations between the mental and the metabolic state have therefore been given greater precision by this work, but not clarified. That in some cases the administration of thyroid extract affects the mental state favourably is confirmed, but the biochemical mechanisms remain obscure.

ORGANIC MENTAL DISORDERS

A review by W. H. McMenemey (1941) of 'dementia in middle age' draws attention once more to a group of conditions which seem to have been very much neglected in this country until D. K. Henderson described them in the first edition of Henderson and Gillespie's *Text-book of Psychiatry*. It is important to recollect in the differential diagnosis of mental disorders in middle life that there are instances in which mental change which would ordinarily be associated with old age appears as soon as the fourth decade is reached and occasionally even earlier. The label 'presenile' is not a bad one. It is still disputed whether there is a simple presenile dementia as such, or whether such instances of gradual but ultimately pronounced failure of memory and judgement in early middle life are always precursors of one of the more characteristic mental states, especially Alzheimer's disease and Pick's disease. Both Alzheimer's and Pick's diseases are characterized sooner or later by focal signs and symptoms, but during life the differentiation between these two types of presenile dementia is difficult if not impossible, although a pneumo-encephalogram may show up the atrophy of the frontal lobes, so characteristic of Pick's disease, for which Nichols and Weigner, quoted by McMenemey, have suggested the name 'idiopathic circumscribed presenile atrophy'. Evidence not yet conclusive accumulates of a familial incidence of Alzheimer's disease, so that this means of differentiating it from Pick's disease is less secure than it was. It is probable that a number of cases diagnosed as Alzheimer's disease clinically are cases of early cerebral arteriosclerosis, but it should be possible to distinguish the latter by its intermittent course. Other rare conditions associated with dementia in middle age are mentioned by McMenemey, such as Huntington's chorea, Creutzfeldt-Jakob disease, and spastic pseudo-sclerosis, of which the histology is a parenchymatous degeneration of the brain with some glial hyperplasia. Mental deterioration associated (1) with primary parenchymatous cerebellar atrophies, (2) with intracranial tumour, especially bilateral tumours of the frontal lobes and tumours of the corpus callosum, (3) with Schilder's disease later in life, or (4) with Marchiafava-Bignami disease (demyelination of the corpus callosum, which is characterized by emotional disorders in the form of instability, irritability or apathy, moral deterioration including sexual misbehaviour, intellectual deterioration and sometimes confusion with focal signs, making it difficult to distinguish it from the other presenile dementias) may all have to be taken into account in differential diagnosis.

NEW METHODS OF INVESTIGATION OR MODIFICATIONS OF OLD TECHNIQUES

Muscle tension

The introduction of the electrical method of recording muscular tension appears timely since there is clinical evidence that some of the effects of war experience can best be summed up as tension states. E. Jacobson (1940) has described an 'integrating neuro-volt meter' which appears to register muscle

tension in the form of variations in action potentials from electrodes placed on selected muscle regions.

Sleep recorders

Disorders of sleep come into a similar aetiological category in many cases, and although the idea is not new, the devising of a new sleep recorder or motiolograph attached to the bed is also timely (B. C. Schiele, 1941).

Brain function

Another need which has been emphasized by war medicine is that which exists for a method of recording the finer failures of brain function as a result of cerebral injury. The Rorschach test promised something in this direction. Recently F. Wertham and L. Golden (1941) have introduced a series of coloured blocks which they invite the patient to build into patterns. They claim that it has a greater diagnostic range and simplicity, and more speed than does the Rorschach method. The material consists simply of coloured blocks, and deductions are made from the number of designs created, the coherence of each design, its concrete or abstract quality, its completeness, harmony, meaning, complexity, compactness, a quality which they call 'distinctness of configuration', realistic or schematic relationship of design to object, indications of movement, choices of colours, shapes, symmetry, repetition, and so forth.

WAR PSYCHIATRY

So far as civilians are concerned the incidence of mental disorders in general has hardly been increased by war experiences. Some psychotic and psychoneurotic conditions have been precipitated, but usually only in obviously predisposed persons. Acute mental reactions have been rare and have consisted either of panic with aimless flight, stuporous immobility, or a kind of crystallized fright reaction with tremors of the limbs and staring eyes and comparative immobility. Amnesias, as a result of war experience, whether among civilians or in the armed forces, have not been common. When they have existed they have been either in people of fairly sound constitution confronted with an experience of overwhelming terror or in people of poor mettle whose amnesia is an escape-device to cover behaviour not altogether creditable. Remote after-effects are less uncommon but not frequent, and consist more often in states of chronic anxiety of psychoneurotic form and less often of mild reactive depressions. Gross hysterical symptoms are seen as a rule only in the very much predisposed and are rare. Probably they have been commoner in recruits of poor psychological constitution in the early stages of their training than in the civilian population as a result of experience of air raids. In children the increase in psychoneurotic conditions has been slight, and is attributable mainly to difficulties of adaptation to new homes in evacuation areas. The problems arise nearly always in those who previously have been psychologically unstable in some fashion. Problems presenting themselves so far in evacuation areas among children have been naturally those which are the most obvious kinds of trouble, especially problems of cleanliness and of aggressive or delinquent behaviour. The delinquency-rate has risen in the bombed areas partly because of the loss of the usual recreational facilities and partly because of the absence of one or both parents on National service. The possibility of later after-effects, as the result of the disorganization of family life, must be awaited.

Treatment

In the acute conditions, both panic and stupor, the use of sedatives in ample dosage is the best method. W. Sargant (1941) recommends in the acute phase phenobarbitone up to 3 grains, sodium amytal up to 15 grains, sodium barbitone up to 15 grains, and paraldehyde 2-4 drachms. Pentobarbital soluble (nembutal)—3 grains repeated at the end of 2 hours—has also been used. If necessary the use of sedatives should be prolonged to effect a continuous narcosis for a week or ten days. For continued narcosis of this sort somnifaine, two cubic centimetres night and morning reinforced by paraldehyde, may be given. As an alternative plan Sargant suggests sodium amytal, 3 grains every 4 hours, or 2-3 drachms of paraldehyde every 4 hours, the

dose being so spaced that the patient is starting to come round at meal times. One hundred ounces of fluid with glucose during the 24 hours is recommended. The urine should be tested for acetone twice daily during the narcosis and the systolic blood pressure also taken. It has been found that in cases in which there has been loss of weight and the patient exhibits chronic anxiety symptoms, insulin in sub-coma doses is often of considerable value not only in increasing weight but in minimizing the somatic symptoms and increasing the patient's confidence. Ten, increasing to 80 or 90 units are given each day, the amount varying with the individual case. The insulin is given at 7 a.m., then the patient usually rests quietly or drowses until roused with a cup of sweetened tea at 10.30 a.m., followed by a meal which includes twelve ounces of potatoes. The doses of insulin are increased up to a level just insufficient to produce hypoglycaemic excitement or coma (Sargant, 1941; G. Debenham, D. Hill, W. Sargant, and E. Slater, 1941). F. W. Brown (1941) has pointed out the importance in the early stages of an acute fright neurosis of getting the history from the patient, provided he is capable of giving it at all, as quickly as possible, thus preventing the development of amnesia for painful experiences. Recovery from these amnesias can be brought about by the intravenous administration of pentothal in 10 per cent solution injected slowly so as to produce brief narcosis without loss of the conjunctival reflex, or sodium amytal (intravenously 3 to 7½ grains) which gives a somewhat more lasting narcosis.

As regards more remote effects of the depressive and psychoneurotically anxious types, time alone usually heals the former, but the latter are apt to take longer to clear up and may in fact, especially in the disposed persons, persist indefinitely. Psychotherapy does not appear to have had much success in those either heavily disposed or who have, as a result of severe fright, acquired what might be called a continued response to bombing, nor is it particularly helpful in those traumatic psychoneurotic states in which no amnesia is involved. In the chronic anxiety responses to war experiences and in the hysterical after-effects when these are obdurate, there is some preliminary evidence from the Burden Neurological Institute that electrical convulsion therapy can be of considerable service (F. Golla, personal communication), but the matter is still *sub judice*.

In the psychiatric problems of evacuated children, the need for child guidance clinics and psychiatric social workers in the reception areas has been amply demonstrated. The need also for hostels for observation of children prior to billeting and for hostels for the more lasting accommodation of the more unstable children is also clear.

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NERVOUS DISEASES

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For various reasons connected with the present war, there is considerably less material to be brought under review than in preceding years, but the amount of new neurological work is still considerable. Throughout the whole of the period now under consideration we have been severed, in a scientific sense, from the neurological institutes and hospitals of the rest of Europe. In the United Kingdom some laboratory work, and a certain amount of special clinical investigations have continued in spite of war and bombs, and in spite of the fact that a very high proportion of neurologists, clinical and laboratory, are attached to the fighting services, or otherwise separated from their usual spheres of investigation. Some of the most important work has been, in fact, directly stimulated by circumstances connected with the war. In America, neurological work has not presumably yet been greatly affected, and a larger part of this annual survey than previously is concerned with publications from the United States. As before, no general account of neurological production is attempted, but the articles chosen for reference are those which either break new ground or which derive some special importance from the nature of their subjects.

ANATOMY

Cerebral hemispheres

Observations made by Scarff by means of electrical stimulation along the superior mesial border of the human cerebrum in 14 consecutive cases indicate that the primary motor area for the upper extremity commonly extends upwards on the lateral surface of the cerebral hemisphere as far as its superior mesial border, while the leg, as a rule, is represented only on the mesial surface of the cerebrum. The author gives a careful review of previous work of a similar kind, including that of W. Penfield and E. Boldrey (1937) and his observations must be regarded as an important complement to theirs. J. E. Scarff (1940) attributes the differences shown between man and the anthropoids in the situation of these functional areas to an upward 'migration' of the primary motor strip, unique to man. It seems probable that this has been influenced by elaboration of new and highly complex functions of the upper limb and the acquisition of speech and other forms of symbolic expression, with corresponding expansion of the cortical areas representing the tongue, mouth, and lips.

Peripheral nerves

H. H. Woollard's discovery of the *intra vitam* staining of cutaneous nerves by methylene blue led to a detailed study of their structure and arrangement by H. H. Woollard, G. Weddell, and J. A. Harpman (1940), and since Woollard's death this has been published, and the work has been carried on by his collaborators. Cutaneous pain is subserved only by fine medullated and non-medullated nerve fibres bearing free endings, and these fibres are arranged in a plexiform interlocking manner. Non-medullated nerve fibres derived from different neurones may lie within the same neurolemma sheath. Several varieties of cutaneous pain can be aroused, even by a single stimulus, but all are subserved by the same nerve apparatus.

The 'accessory' innervations to encapsulated touch receptors in the skin and to nerve endings subserving pressure, cold, and proprioception from tendons are morphologically similar to the nerve fibres and endings subserving pain. Fine somatic nerve fibres bearing free endings similar to those subserving pain in the skin occur in the adventitia of blood vessels. From tendon substance pain can only be excited near musculo-tendinous junctions,

and it is probable that there is an accessory innervation of the neurotendinous endings of Golgi in man and that stimulation of the accessory fibre or ending gives rise to pain. Pursuing this study, Weddell has made interesting and important observations on the pattern of the cutaneous pain-innervation. The nerve plexuses in the skin of man, monkey, rabbit, and *Acanthias vulgaris* are constructed on much the same pattern. It is such that in general each unit area is evenly innervated by fibres which approach it from all directions. A single nerve fibre in the dorsal nerve at the base of the ear of the rabbit breaks up into terminal ramifications which are distributed to approximately three hundred hair follicle groups, and cover an approximately circular area 1 cubic centimetre in diameter. Each hair follicle group and each hair is innervated by at least two separate nerve fibres, the terminal ramifications of which are evenly interlocked. After section of approximately one-quarter of the dorsal nerve, degenerating nerve fibres can be seen throughout the whole extent of the skin of the dorsum of the ear.

In man a single isolated superficial nerve net in a hypo-algesic area of skin from the dorsum of the hand covers an approximately circular area, 0.75 centimetre in greatest diameter. This distance corresponds to the threshold of two point discrimination for pain in a similar normal area. There is evidence to suggest that cutaneous nerve trunks, on approaching the skin, rapidly disperse and ramify over wide areas before giving rise to cutaneous nerve plexuses, and that the fibres approach their terminal areas from all parts of the periphery. The patterns of sensory loss and recovery shown after some complete nerve trunk lesions and interruptions are in conformity with this view.

The vertebral veins and their connexions

The connexions of the vertebral veins have been studied by Batson in the human cadaver and in the living monkey by the method of injection of radio-opaque material and subsequent radiography. The veins surrounding the vertebral column and those of the retrothecal plexus constitute a more or less independent system of veins which provides a pathway from the pelvis up to the intracranial sinuses and cerebral veins. Using a latex rubber mass for the routine injection of cadavers for dissection, and injecting into the dorsal vein of the penis, O. V. Batson (1940) expects to find fairly well filled such veins and sinuses of the cranial cavity as the superior longitudinal sinus, the cavernous sinus, Trolard's anastomotic vein and others. The paper referred to is accompanied by some very convincing skiagrams. The vertebral venous system has connexions with the visceral and somatic veins, particularly in the pelvis and in the chest. It is devoid of valves and the flow in it is easily reversible. Under conditions of straining, blood is forced into it from the visceral veins. It may act either as a venous pool or as a by-pass for the other vein systems. Batson points out that it may provide a vehicle for the passage of malignant or pyogenic material and so may account for the situations of some metastases from pelvic malignant growths or infections, the sites of which are otherwise difficult to explain.

PHYSIOLOGY

The thalamus and cortical activity

In previous reviews reference was made to the connexions of the thalamus and the influence of the thalamus on the activity of the cerebral cortex. F. H. Lewy and G. D. Gammon (1940) examined the influence of afferent systems on the spontaneous activity of portions of the cerebral cortex of the cat, under nembutal, as indicated by electric potentials. They found that such activity depended on intact sensory pathways. It was not influenced by removal of the cerebellum, the opposite cerebral hemisphere, or other lobes of the same hemisphere in which the area examined was situated, but it was abolished by (1) section of the brain at the level of the colliculi, (2) destruction of the thalamus, or (3) cutting the thalamo-cortical radiation. J. G. de Barenne and W. S. McCulloch (1941) obtained similar results. Even incision around the area under examination did not put an end to its spontaneous

activity, but the latter was abolished at once by destruction of the corresponding portion of the lateral nucleus of the thalamus or of the thalamo-cortical radiation. It is thus clear that the thalamic influences are essential for cortical activity, and are in fact almost the only connexions that are essential.

The basal ganglia

S. A. K. Wilson in his description of the disease which bears his name prematurely drew deductions from his clinico-pathological material as to the normal functions of the lenticular nucleus and globus pallidus, but when he subsequently made experimental lesions in these structures in monkeys he failed to obtain any symptoms comparable to those of progressive lenticular degeneration in man. Since then other experimental workers have had similar fortune. Wilson, however, pointed out that some of the monkeys preferred to take nuts and bananas with the homolateral limb, or in climbing about their cage they showed 'the least awkwardness or clumsiness with the contralateral limb'. Recently Bottrell has made similar observations (unpublished). As means of examination of experimental animals become more detailed it is becoming clear that destructive lesions in the basal ganglia do give rise to certain disturbances of movement and posture which though minor are of the type which are associated with extra-pyramidal disease in man. E. G. T. Liddell and C. G. Phillips (1940) described their results as follows. Electrolytic lesions were made in the basal ganglia of 26 cats. The leading physical sign of such lesions was a slight but persistent hypertonia of extensor muscles in the contralateral limbs. The hypertonia was not evident in the gait, and did not become manifest unless the animal was mentally at rest, and was held up so that the limbs hung freely. Other physical signs were (1) delayed flexor reflex, (2) defective placing reactions, (3) flexor hypertonia of the ipsilateral side, and (4) defective closure of the contralateral eyelid. De-afferentation appeared to cause some temporary reduction of the extensive hypertonia. Control experiments consisting of the passage of electrodes into the basal ganglia without electrolysis (7 in number) and of the production of lesions elsewhere than in the basal ganglia (10 in number) were unproductive of permanent physical signs.

CLINICAL NEUROLOGY

Effects of blast

Clinical neurology has been less influenced than might have been anticipated by problems arising from the war. The effects of the blast of high-explosive bombs on the central nervous system have seldom been observed clinically. A peculiar apathy in some patients who have been exposed to blast has been attributed to blast effects on the brain, as also has a state of extreme and eventually fatal shock, but there is little pathological support for these views. States of flaccid paralysis very similar to those produced by poliomyelitis have been attributable in rare cases to the effects of blast on the spinal cord. In two such cases known to me full recovery occurred.

Trichiniasis

Small epidemics of trichiniasis in the United Kingdom, more or less directly attributable to the conditions of war, have been characterized by the frequency of cerebral symptoms, of which hemiplegia, monoplegia, and diplopia have been the most frequent. Convulsions and meningitic signs have also been described. J. H. Sheldon (1941) observed neurological signs in 13 out of 76 cases. These included focal pareses and signs of general inflammation suggesting meningitis or encephalitis. In conjunction with such signs the cerebro-spinal fluid may not present any abnormality, or there may be pleocytosis and increased protein content.

Headache and migraine

Experimental studies on headache have been made by G. A. Schumacher, B. S. Ray, and H. G. Wolff (1940), using histamine to provoke the symptom, as was done by Pickering and Hess. The former group of workers anaesthetized the superficial tissues of the head and found that the headache caused by injection of histamine was not influenced by this procedure. Compression of arteries had some effect, but the intracranial and dural arteries play only a minor part

in contributing to the pain. In patients with complete section of the sensory root of the 5th cranial nerve, resulting in unilateral hemi-analgesia of the face and anterior half of the scalp, histamine headache was not induced on the denervated area, but did occur elsewhere in the head, and similarly in a subject with complete hemi-analgesia of the face and head, resulting from a head injury, headache strictly confined to the normal side was induced by histamine. Histamine headache was absent in the back of the head on one side, but was present elsewhere in the head in two subjects with lesions of the cervical portion of the cord, causing unilateral occipital analgesia. Section of the 7th and the 9th cranial nerves, and of both sympathetic trunks, in different subjects had not any effect on subsequently induced histamine headaches. The writers concluded that the histamine headache does not depend on the integrity of sensation from the superficial tissues. Although there may be other less important afferent pathways for the conduction of impulses interpreted as headache after injection of histamine, (a) the 5th cranial nerve on each side is the principal afferent pathway for headache resulting from dilatation of the supra-tentorial cerebral arteries and felt in the fronto-temporo-parietal region of the head and (b) the upper cervical nerves are the most important afferent pathways for headache resulting from dilatation of arteries of the posterior fossa and felt in the occipital region of the head.

The headache of migraine

Subsequently Schumacher and Wolff (1941) found that histamine headaches were abolished by increasing the intracranial pressure and they attributed this effect to the added extra-mural support given to the arteries at the base of the brain, and regarded it as further evidence that histamine headaches result mainly from the dilatation and distension of these arteries. They found that the headaches of migraine were not reduced in intensity by increasing intracranial pressure, and thought that they originated in distension of extra-cerebral arteries. In a subject, who experienced somewhat prolonged visual disturbances preceding the headache, they proved that inhalation of sufficient amyl nitrite to give a feeling of throbbing in the head, but not to cause a fall in blood pressure, abolished the scotomas, but inhalation of a larger amount, with a severe fall in the general blood pressure, greatly increased the visual disturbance. Their deduction was that the pre-headache phenomena were due to constriction of cerebral arteries and were augmented in association with the fall in blood pressure, because of the accompanying decrease in cerebral blood flow. They considered that the essential phenomena of migraine resulted from a complex dysfunction of cranial arteries and represented contrasts in vascular mechanisms in the different vascular beds—constriction in cerebral arteries, followed by dilatation of the branches of the external carotid arteries.

Epilepsy

Pursuing their studies of epilepsy by means of the electro-encephalogram W. G. Lennox, E. L. Gibbs, and F. A. Gibbs (1940) have applied this method to the problem of the inheritance of epilepsy. Electro-encephalographic tracings have been made of the parents, siblings, and children of 94 patients who have both clinical epilepsy and cerebral dysrhythmia. The relatives numbered 183. Tracings were made simultaneously from six areas of the cortex. Abnormal records were obtained in 60 per cent of the relatives of patients and in 10 per cent of a control group of 100 persons who had no near relative with epilepsy. In 55 of the families records were obtained from both parents. In 35 per cent of these the records of both parents were clearly abnormal. In only 5 per cent were the records of both parents unmistakably normal. Dysrhythmia occurred as often among the relatives of patients with so-called symptomatic epilepsy as among the relatives of patients with 'essential' epilepsy. The data included 5 families in which there were similar twins with seizures or dysrhythmia. In each pair of twins there was a similarity of the fundamental rhythm, although seizures in both twins occurred in only one pair. The authors believe that evidence indicates that the dysrhythmia of epilepsy is inheritable and that such dysrhythmia represents a predisposition

to epilepsy or some allied disorder; dysrhythmia may prove to be a dominant trait.

Simmonds's disease

H. L. Sheehan (1939) has shown that in women who have a severe collapse at delivery and die during the puerperium there may be extensive necrosis of the anterior pituitary, which appears to be due to thrombosis of the vessels. His analysis of published necropsy reports of patients with Simmonds's disease dating from parturition some years earlier showed that they had old necrotic lesions in the anterior lobe, which were easily distinguishable from the atrophy and fibrosis found in cases unconnected with pregnancy. In collaboration with R. Murdoch, Sheehan later in the same year produced convincing evidence that if a patient survives a collapse at delivery she may subsequently show manifestations of pituitary insufficiency. The severity of these disturbances bears a definite relation to the severity of the collapse, and the symptoms may involve almost any system of the body. During the first few weeks after delivery they are, as a rule, overshadowed by the patient's obstetrical condition. In severe cases there is usually complete absence of mammary activity during the puerperium; there may be hyperinvolution of the uterus and genital atrophy resulting in sterility, with loss of the axillary and pubic hair, asthenia, psychological change and anaemia. Later the patient may appear to be myxoedematous or prematurely senile. In the majority of patients the weight is unaltered, but exceptionally, loss of appetite leads to emaciation and death. In milder cases there may be various menstrual disturbances, thinning of the hair, debility, anaemia, hypersensitivity to cold, and mild changes in character, such as listlessness, loss of initiative, and forgetfulness. Sheehan and Murdoch have also demonstrated that in patients who have had a post-partum necrosis of the pituitary a subsequent pregnancy is possible if genital atrophy has not taken place, and that in the absence of any further collapse at delivery a subsequent pregnancy or even miscarriage greatly improves or completely cures the symptoms of pituitary insufficiency. They suggest that the part of the pituitary which escaped the necrosis undergoes the normal physiological hypertrophy during the second pregnancy and does not return to its previous size after delivery. The rational treatment of this condition is therefore to encourage another pregnancy, and if genital atrophy is present the administration of sex hormones may make this possible. The greatest care must be taken to avoid a repetition of the collapse.

Venous thrombosis in the central nervous system

Following the discussion referred to in last year's review, J. P. Martin and H. L. Sheehan (1941) have described in detail their observations on the clinical features and pathology of thrombosis of the cerebral veins. Convulsions and hemiplegia were the usual symptoms, and areas of softening were found on the surface of the brains in fatal cases. Many of the patients made good recoveries. Since then Martin (1941) has given a clinical description of cases believed to be instances of thrombosis of the sagittal sinus following child-birth. The symptoms were those of intracranial pressure, together with those of thrombosis of one or more cerebral veins. Martin suggests that a fragment of clot translated from the pelvic or femoral veins by way of the vertebral venous system (see p. 89) lodges in the sagittal sinus and forms the nucleus of the clot which is developed there.

EXPERIMENTAL PATHOLOGY

Experimental cerebral concussion

An important piece of work, and one stimulated directly by the circumstances of war, is that of D. Denny-Brown and W. R. Russell (1941) on experimental cerebral concussion. Denny-Brown had previously shown that the objective phenomena accompanying concussion in man were those due to disturbances of function in the brain stem, viz. changes in respiration, pulse and blood pressure, and loss of the corneal and other brain-stem reflexes. In experimental work, the animal being necessarily anaesthetized, it is impossible to study the state of consciousness after the blow has been inflicted, but there can be little

doubt that when the phenomena which normally accompany loss of consciousness occur with sufficient intensity to abolish reflexes, it is justifiable to assume that loss of consciousness would have occurred had the animal not been anaesthetized. Judged in this way experimental concussion in the cat, dog, and monkey shows features rendering it directly comparable with cerebral concussion as observed clinically in man. Denny-Brown and Russell define concussion as a direct traumatic paralysis of nervous function without vascular lesion, the paralysis persisting for a varying period according to the type and severity of the injury. One of their first observations was that concussion was produced much more easily if the animal's head was able to move in the direction of the impact. This is an observation of basic importance, which has been missed by earlier investigators. Denny-Brown and Russell deduce that there are two mechanisms which may cause concussion—acceleration and compression. Provided movement is allowed, pure concussion can readily be produced by subjecting an animal's head to a blow producing a sufficiently high rate of change of velocity ('acceleration concussion'). Concussion produced by a crushing injury, striking the head while it is supported on a hard surface ('compression concussion') requires a much greater force to produce the same effect and the mechanism by which concussion results is somewhat different. Another early observation was that a minimum velocity of impact was required. A larger momentum was ineffective if this critical velocity was not reached. 'Acceleration concussion' results in the monkey and cat when the head is struck by a heavy mass with velocity approximately 28 feet per second; in the cat the velocity of 23 feet per second was sometimes sufficient, but this was exceptional. These findings will lead to and inspire further work. 'Acceleration concussion' is a convenient term, but possibly factors other than acceleration are concerned; for instance, a minimum displacement is probably required. Denny-Brown and Russell do not attempt to examine the cause for their finding that there is a minimum adequate velocity, but such a velocity is presumably required to overcome the efficient mechanical buffering of the brain.

Additional discoveries

Other findings are as follows.³² Experimental concussion causes transient reflex paralysis of the respiratory and vasomotor mechanism, corneal and pinna reflexes, reflex deglutition, and the other reflex motor mechanisms of the pons and medulla. The vasomotor and respiratory centres, while not available to reflexes during this concussive reflex paralysis, are stimulated by the injury, unless the trauma is extremely severe when a phase of complete paralysis results. Acceleration concussion is obtained in the decerebrate animal, both with and without section of the 8th cranial nerves. It can also be obtained with the animal under artificial respiration. The effect on the brain stem is therefore not dependent on the fore-brain or on vestibular influences; nor does it depend on respiratory failure. In a further series of experiments Denny-Brown and Russell found that acceleration concussion was not accompanied by any significant change in the intracranial pressure, whereas in compression concussion a great increase of pressure applied with high velocity was required. When failure of blood pressure results from a severe head injury, the mechanism appears to be identical with that of primary surgical shock. Both are associated with peripheral vasoconstriction and paralysis of the venous side of the circulation. Such shock is greatly facilitated by haemorrhage, or by repeated concussion.

Death from acceleration concussion

Death from acceleration concussion is due to failure of blood pressure. Though this may arise from failure of the vasomotor centre during the paralytic phase of severe injury the essential lack of recovery arises from the effect on the vago-glossopharyngeal mechanism in inducing 'primary shock'. Death may thus occur as a delayed effect when the stage of recovery from paralysis has begun. The reflex compensatory mechanism then makes inadequate response to the fall in blood pressure.

Paralytic phenomena

The paralysis of concussion is immediate. Further, it is associated experimentally with an increased blood flow through the brain and brain-stem. There is not any evidence of vascular spasm in the brain during, or resulting from, acceleration concussion. Denny-Brown and Russell conclude that the paralytic phenomena of concussion are due to a direct generalized physical injury to the neurones. This injury causes immediate loss of function, but is reversible. The mechanism by which the neurones are damaged in acceleration concussion must be of great complexity.

Haemorrhagic lesions

Haemorrhagic lesions, both extracerebral and intracerebral, which occur in very severe injuries, indicate distortion of stress, but not necessarily identical with that which causes concussion. The necessity for movement in the production of *contre-coup* lesions and concussion indicates the part played by the inertia and momentum of the brain, as compared with skull, in both of these conditions. Petechial haemorrhages are commonly found in the grey matter and under the pia mater of the upper segments of the cervical spinal cord, but the effect of these contusions of the medulla and cervical cord can be dissociated from the primary effects due to concussion, for they cause a delayed embarrassment or failure of respiration according to their extent, this delayed effect being observed to reach a maximum 1–2 minutes after the blow. Very small haemorrhages in this situation do not interfere with recovery from concussion, and clinical evidence strongly suggests that they can occur without concussion. Contusions in the cerebral hemispheres have not any effect on the bulbar centres unless a great increase of intracranial pressure is developed as a result of haemorrhage in the bruised area. This effect is also delayed in onset, and reaches a maximum in from 1 to 4 minutes after the injury.

Duration of paralysis

When the intensity of head injury is increased over and above the threshold which produces concussion, the effect is to prolong the paralysis of concussion, although still no lesion is caused. The rate of recovery, therefore, of the neuronal damage is proportional to the severity of the injury. The authors present no data relating to the impairment of function of the cerebral cortex following experimental concussion, but it seems very probable that it behaves as do the reflex mechanisms studied.

Influence of the shape of the skull

It may be observed in applying these results to man that the compression factor may be greater in man than in the animal because of the more elongated shape of the human head, the change of pressure produced by deformity being greater the more the skull deviates from the spherical.

SURGERY**Repair of peripheral nerve lesions***Plasma-fibrinogen technique*

J. Z. Young and his co-workers (1940) have devised a method of soldering the ends of a divided nerve with a preparation of plasma reinforced by additional fibrinogen. This is mixed just before use with a little strong tissue extract (chicken embryo extract). The method consists simply in holding the cut stumps together and pouring this preparation around them. In about $\frac{1}{2}$ –2 minutes, according to the age of the plasma and the strength of the extract, the plasma clots into a firm jelly which sticks to the nerves and holds the ends together. With their technique little or no plasma penetrates between the cut stumps. During the subsequent days the plasma-solder is dissolved, but it remains long enough to allow a firm union to be established between the approximated nerve-ends. In rabbits reopened two or three weeks after operation, no trace of it is seen.

Histological studies show that the junctions made by the plasma method are readily crossed by nerve fibres, and there are none of the whorls and deviation of large bundles of fibres which are unavoidable with stitching unless the

epineurium alone is sutured. New fibres grow slightly faster across a plasma-solder junction than across a sutured junction. The distance of outgrowth of axons in the peripheral stump can be determined in the anaesthetized animal by pinching the nerve to discover the most peripheral point from which reflex responses can be obtained. In this way it has been established that in the rabbit there is a latent period of 8.1 days before the plasma junction is crossed. Having entered the peripheral stump the new fibres grow at the rate of 3.9 millimetres a day. When the nerve fibre arrives at the muscle there is a long delay before voluntary movement is possible. Young estimates the delay at the motor end-plates in the rabbit at 22 days. Delay at the skin he estimates at about a month. In the regeneration of the nerve the Schwann cells of the peripheral stump play an active part. If the stumps of a divided nerve are allowed to remain separated from each other, outgrowths occur from both the central and the peripheral stumps. In the latter, growth is at least as vigorous as in the former and consists of Schwann cells, which grow centrally as broad strands of tissue and join up with the central stump. The average rate of outgrowth from the peripheral end is about 0.45 millimetre a day and may be as much as 1 millimetre a day. There is every reason to believe that small gaps in divided nerves can be bridged naturally in this way.

Nerve grafts

J. Z. Young, W. Holmes, and F. K. Sanders (1940) have also made experiments with different kinds of nerve grafts, using the plasma-solder method of apposition at both junctions. Auto-grafts were the most successful, and no advantage was observed as a result of pre-degeneration. A fresh auto-graft provides a medium for the growth of new fibres which is only slightly less satisfactory than a normal peripheral stump. It is recognized, however, that the presence of two junctions may decrease the extent to which new fibres reach appropriate end organs. Cable grafts consisting of several strands of a small nerve are also very successful; the strands can first be made into a bundle with plasma and then the whole is fixed in place without the necessity of numerous stitches. This very promising work continues and the methods described are already being utilized in surgical practice.

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breeds in small pools of water near human habitations, as stressed by M. A. Barber (1940). In South Africa this dangerous vector is reported to have been carried to new areas by motor car. The war conditions, and especially the wide use of aeroplanes, may easily be the cause of the further disastrous conveyance of malaria-carrying anopheles to new areas.

Prophylaxis of malaria

In hyper-endemic malarial areas, such as exist in large parts of tropical Africa, the children become infected early in life, and those who survive gradually develop such a tolerance to the malarial parasites that they seldom suffer from actual malarial fever, in spite of harbouring the parasites in their blood up to adult life. The older children and adults do not acquire a true immunity because, if the malarial parasites disappear completely from their blood, they become prone to fresh infections; this condition of tolerance is called *premunition*. D. B. and Margaret E. Wilson (1941) in Tanganyika and others therefore advise that attacks of malarial fever in the indigenous population of such hyper-endemic areas should receive only short courses of treatment with quinine or mepacrine to stop the febrile attacks, without destroying all the parasites and so rendering the patients liable to fresh infection. On the other hand, infections among highly susceptible races, such as Europeans, coming to hyper-endemic areas from non-malarious ones, should be thoroughly treated, because relapses may be dangerous, and also because repeated attacks of malaria strongly dispose to the still more dangerous blackwater fever complication of malaria. This applies to our military forces serving in north-east Africa and Palestine and Syria.

The question whether or not a true immunity to malaria can be produced has recently been discussed by Sinton, who holds that two factors are involved. The first is an anti-parasitic one, through the phagocytic action of the macrophage system, which tends to keep organisms at too low a level to permit of active clinical symptoms appearing. The second acts through a humoral production of antitoxic elements, which reduces the power of the toxins formed by the parasites to produce clinical symptoms. The residual immunity after an attack of clinical malaria is greatest in the case of *P. ovale* infections in Africa, it is considerable after *P. vivax* benign tertian attacks, and least after those of *P. falciparum* of malignant tertian malaria. J. A. Sinton (1938) therefore advocates radical cure when the chances of reinfection are slight, clinical cure after each attack when there is frequent or constant exposure to reinfection, to allow of the gradual production of immunity, and clinical prophylaxis when exposure to infection is of a temporary character, as is often the case under war conditions. Military forces can thus be kept fit for active service in spite of unpreventable infections that are kept below a clinical level by regular prophylactic doses of quinine or mepacrine, preferably the former. Experience in Panama, for example, showed that clinical malarial fever was almost abolished by giving 15 grains of quinine daily or mepacrine 0.1 gramme thrice daily for 5 days, followed by 0.01 gramme of pamaquin (plasmoquine) twice a day for 5 days to all carriers of malaria found during monthly surveys. It must, however, be borne in mind that such prophylactic treatment only suppresses the active manifestations of malaria, but does not prevent infection; so that when the drugs cease to be given, e.g. when the patient is no longer required for military or other purposes, malarial attacks are liable to occur and demand radical and prolonged treatment for their permanent cure. Experience in the British Army in India, however, shows that the administration of a course of small doses of pamaquin after one of quinine or mepacrine greatly lessens the number of subsequent relapses. By this means the disabilities extending up to about two years, so often seen among our soldiers returning from the Near East in the 1914-18 war, should be greatly reduced in the future.

Transmission of malaria by blood transfusions

In view of the extensive use of blood transfusion for shock in war, and in civilian injuries due to bombs, a word of warning is advisable regarding the danger of transmission of malarial infection, if the donor has suffered from

malaria during service in a malarious country; for E. L. Hutton and P. G. Shute (1939) pointed out that preservation of blood at low temperatures does not destroy the malarial parasites. They suggest that the danger may be much lessened if such blood donors take 10 grains of quinine once a week; this measure will also go far towards their protection from febrile relapses. The frequency with which drug addicts in Egypt and in China have been reported to have been infected by malaria, by the use of the same syringe for injections without proper disinfection, emphasizes the possible danger from blood transfusions.

In British Guiana G. Giglioli (1939) has recorded data to show a close relation between an increase in the percentage of persons showing enlargement of the spleen and a lowered birth-rate, as well as with increased still-birth and infant mortality rates. As early as 1904, in my report on fevers in the Dinajpur District of Bengal, I pointed out the high mortality rate during the first few days of life among infants born to malarial subjects.

Treatment

No important recent advances have been made in the use of synthetic drugs in malaria. Further reports have not confirmed the value of the sulphonamide group of drugs in malaria, in which they do not appear to be well borne. The Ascoli treatment of malarial spleens by intravenous injections of adrenaline, so much advocated by Italian writers, has been condemned as valueless by G. Casini (1939) and by G. Marotta (1939), working respectively in Sardinia and Rome.

During the war of 1914-18 I suggested, as the result of a few trials, the intravenous injection of tartar emetic against the gametocyte stage of malarial parasites, but variable results were recorded by other workers. It is therefore of interest to note that R. de Nunno (1938) reports that the injection of a 1 per cent solution of tartar emetic intravenously on alternative days, up to a total of 120 to 200 cubic centimetres, much diminished the development of gametocytes, which lost their normal appearance and rapidly disappeared from the blood, together with loss of the power of the patient's blood to infect anopheles and so convey the disease to others. G. Carra (1940) also reports success in the treatment of primary attacks of malaria with antimony tartrate intravenously, as well as remarkable effects in reducing the size of the spleen and improving the general condition of the patients. Antimony salts therefore appear to be worthy of further trial in malaria.

Methods of control

Paris green remains the best larvicide against that stage of anopheles, and pyrethrum the most useful insecticide for destroying adult mosquitoes in houses and barracks in malarious areas. They are of great value in protecting stationary military camps, but have only a very limited use in the case of rapidly moving military forces. It is usually laid down that an area of half a mile around cantonments or camps should be freed from anopheles larvae, but this may sometimes prove insufficient. Thus, P. C. G. Adams (1940) in Northern Rhodesia found that the dangerous *A. funestus* can fly four and a half miles down wind and one and a half at an angle of 30° up wind, and in Malaya R. B. Wallace (1939) showed that *A. maculatus* can traverse 1½ miles in search of a blood feed. For such tests A. Vargas and F. Freire (1940) found that if larvae are immersed in 0.025 to 0.050 per cent solution of methylene blue for 18 to 48 hours, the adult insects developed from them show a definite blue coloration, allowing their range of flight to be traced.

TYPHUS FEVER

In the 1940 Critical Survey the danger that the war might result in increased prevalence of epidemic louse-borne typhus fever was pointed out. Since then the extension of the destruction and scarcity to the Balkan States and to Russia has enhanced the probability of wide-spread epidemics in eastern Europe during the winter of 1941-2. Indeed in the middle of 1941 typhus was reported to be prevalent in much-suffering Poland, and even to have attacked German soldiers.

Delousing is the most essential preventive measure, but is apt to break down under war conditions. The *Ministry of Health Memorandum No. 230* (2d., published by the Stationery Office) is instructive on this subject. Attendants on cases of these fevers require special louse-proof clothing for their protection, as a single louse may infect. These insects become infective 8 days after biting typhus patients between the fifth day of fever and the terminal crisis. Special hospitals with elaborate delousing and disinfecting arrangements are necessary for the control of outbreaks and have been described by R. Dujarric de la Rivière (1939). The rooms should be disinfected daily by washing down with 5 per cent sodium carbonate solution and fumigation with sulphur. Bedding and clothing may be disinfected by boiling in the same solution, or by steam or sulphur fumigation. G. Blanc and M. Baltazard (1940) have shown that the virus of murine typhus persists in a virulent form in the dried faeces of fleas for 2 years; this may account for transmission of the disease from one cold season to another.

Preventive inoculation against typhus was discussed fully in the 1940 Critical Survey (p. 76), and since then little advance has been made. It was then pointed out that murine living vaccines attenuated with bile produced lasting immunity in the indigenous races, but were dangerous in Europeans. On the other hand, the harmless killed vaccines produce less effective immunity. It has been suggested that partial immunity produced by killed vaccines might safely be followed by an attenuated living vaccine to strengthen the immunity, but the length of time required would militate against the value of this plan during epidemics. No effective treatment of typhus is available, although the use of convalescent serum has been suggested.

Altogether the prospects of controlling typhus and relapsing fever epidemics in the war-stricken areas of eastern Europe do not appear to be bright. Nor would it be surprising if the aggressor states of central Europe find it beyond even their autocratic powers to save their impoverished countries from an invasion by typhus, and perhaps also relapsing or famine fever and other communicable disease.

YELLOW FEVER

The most important recent development regarding the incidence of yellow fever is the extension of the proved infected areas over large regions of north-east Africa. Thus G. M. Findlay (1941) states that the known endemic area now stretches from the west coast of Africa just north of Cape Verde along the southern border of the Sahara desert to the Anglo-Egyptian Sudan. It then passes southward as far as or beyond the Sudan-Abyssinian border and through western Uganda, and back again across the Belgian Congo to the west coast of Africa at the mouth of the Congo river. This extension enhances the danger of its spread to the coast of East Africa, and thence to India and the Far East, which has so long been dreaded. For some years past an International Convention has controlled the air services in the endemic area of yellow fever with a view to prevention of its spread by aeroplane, but here, once more, the extensive involvement of north-east Africa in the totalitarian war may easily prove a fatal handicap to the control of this dreaded disease. Findlay advises the wide use of the well-established immunization against yellow fever, to protect the masses of the population in the threatened areas of East Africa, as the best method of control.

CHEMOTHERAPY

THE SULPHONAMIDE COMPOUNDS

Sufficient trials of this potent group of drugs in tropical diseases have now been made to allow some estimate to be made of their value. Most promising results have been obtained in the deadly *bubonic plague*, against which there has not hitherto been any effective remedy, except to some degree from the use of anti-plague serum. The Bombay workers, S. S. Sokhey and B. B. Dikshit (1940), have tested some of these drugs in highly susceptible mice, septicæmic infections in which are almost invariably fatal. They found that sulphathiazole in small doses saved nearly 80 per cent of mice treated before septicæmia had set in, and, still more striking, up to 90 per cent of septicæmic infections in

mice were cured by large doses of this drug. Subsequently the Bombay workers treated 237 cases of plague in the Province of Bihar, which were divided into three series and treated with anti-plague serum, sulphapyridine, sulphathiazole, with mortalities of 28, 24, and 15 per cent respectively against one of 52 per cent on control cases. The serum could not be given in doses of 20 cubic centimetres and upwards without the occurrence of alarming symptoms in some cases, so it did not have a full trial. The above results from the new drugs are statistically significant of material benefit, so if they are confirmed yet another life-saving advance will have resulted from chemotherapeutic animal experiments against one of the most ancient and dreaded of epidemic diseases.

In *undulant fever*, on the other hand, early favourable reports on the use of these drugs in small series of cases have not been confirmed by further experience.

The success of sulphonamides against *B. coli* infections has led to its trial against the closely allied micro-organisms of bacillary dysentery, with promising results in a few instances. Thus, R. Reitler and K. Marberg (1941) treated 20 severe cases, verified bacteriologically by the isolation of Shiga, Flexner, and other types of organisms. They gave 2-gramme doses of sulphapyridine three or four times a day for 2 to 4 days, together with sodium bicarbonate to counteract nausea. They report a fall of temperature to normal within 24 hours, and normal stools within 1 to 4 days, usually in 1 day. After the stools became formed, dysentery bacilli could no longer be found in them. E. K. Marshall, Jun., A. C. Bratton, Lydia B. Edwards, and Ethel Walker (1941) in the United States of America report good results in early cases of bacillary dysentery in children from the administration of from 0.05 gramme of sulphanilylguanidine per kilo body weight, so this drug also appears to be worthy of further trial.

Sulphonamide compounds are also reported to be of value in the treatment of cases of inguinal ulcerative granuloma before the development of fistulas, and in the dangerous streptococcal complications of filarial lymphangitis.

Diamidines in protozoal infections

The researches of E. M. Lourie and W. Yorke (1939) in Liverpool on the value of diamidines in trypanosomal infections in mice and rabbits have led to a trial of 4:4'-diamidinostilbene in sleeping sickness cases in Nigeria. R. D. Harding (1940) found this drug to be of considerable value in first stage cases, with the great advantage of not being harmful to the eyes. Unfortunately in the later stages with cerebrospinal involvement the results were unsatisfactory, so tryparsamide remains the most effective drug in such cases.

Trials of the new diamidine compound in kala-azar infected hamsters produced good results, and this led to its use in human infections. Eight daily intravenous injections of 1.0 milligram per kilo body weight produced rapid recovery in kala-azar cases in the Sudan, where the disease has been found to be much less amenable to antimony treatment than the Indian variety. Moreover, no relapses were noted during the 6 months after treatment, so it will be of especial value in the occasional cases of kala-azar which prove resistant to antimony treatment.

Chemotherapeutic experiments with a view to the discovery of effective and cheap remedies for kala-azar will be facilitated in future by an interesting observation of R. O. A. Smith, K. C. Halder, and I. Ahmed (1940) in Calcutta. Previously feeding infected sandflies on hamsters only occasionally produced infection after the very long incubation period of about a year. It has now been shown that *P. argentipes*, fed on raisins after a preliminary feed on the blood of a kala-azar patient, commonly develop blocking of the oesophagus with the flagellate stage of the *Leishmania donovani*, much in the way that plague fleas may become blocked with plague bacilli. Such blocked sandflies have been found capable of infecting five successive hamsters, with far shorter incubation periods than in the former occasional infections of those animals. These convenient little rodents will therefore be more easily available for the study of drugs for the treatment of kala-azar.

Taken altogether steady progress is being made in the study of tropical diseases, in spite of the hampering effects of the unprecedentedly destructive war.

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VENEREAL DISEASES

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PROPHYLAXIS

According to R. Cautley, G. W. Beebe, and R. L. Dickinson, in 1934 and 1935 C. I. B. Voge tested more than 2,000 rubber sheaths and found that more than 50 per cent of them were defective. The Council on Pharmacy and Chemistry of the American Medical Association state that as it is recognized that prophylaxis by chemical agents is not completely reliable, the United States Food and Drug Administration have informed manufacturers of condoms that all articles for the prevention of venereal diseases are subject to the provisions of the Food and Drug Act, and in the year ending June 30, 1939, they seized 75 consignments of prophylactics; the result has been a general improvement in the quality of condoms sold in the United States of America.

INCIDENCE

In the Critical Survey for 1940 it was stated that almost a year after the start of the war there was no statistical evidence of any great increase in the incidence of venereal diseases in Great Britain. A closer survey than was then possible has shown that in 1940 in England and Wales the increases in syphilitic infections were 27 per cent in males, including those in the Services, and 12 per cent in females. The rates of incidence of gonorrhoea could not be determined because of the large numbers of these cases now treated privately. It is encouraging that in the Army stationed in Great Britain in 1940 the rate for all forms of venereal diseases (8.4 per 1,000) was less than one-third of the average for 1915-18 (29.6).

SYPHILIS

Infectivity and age of infection

It is commonly believed that the infectivity of syphilis diminishes with the age of the infection until by the end of five years it has practically disappeared. This has been confirmed substantially, though not completely, by two recent reports. P. A. O'Leary and D. H. Williams (1940), of the Mayo Clinic, report on an investigation of 1,175 married couples in each of whom at least one partner had syphilis. They concluded that it must be accepted that infectivity persists during the first five years but that thereafter it lessens and at the tenth year it approaches vanishing point. L. L. Klingbeil and C. E. Clark (1941) examined the spouses of 226 syphilitic patients from this point of view, and in 25 cases, 13 untreated and 12 treated, in which the disease had been present for four or more years before marriage, the spouse had escaped.

Infectivity of vaginal and uterine secretions

H. Pariser (1941), as a result of inoculations of mice with vaginal and cervical discharges of 25 syphilitic women, has concluded that *S. pallida* appears in the vagina only during menstruation or when there are syphilitic lesions in the uterus and vagina, or in either of these organs alone.

Diagnosis

Cytology of the blood

U. J. Wile, R. Isaacs, and C. W. Knerler (1941) studied the blood cytology in 36 cases of early untreated syphilis in human beings and in 9 syphilitic rabbits. Although confirming previous work on this subject in finding a mild secondary anaemia, monocytosis, eosinophilia, and an occasional leucocytosis, they note as a feature which has not hitherto been described that in 80 per cent of the cases there were plasma cells in the blood films; their presence was

attributed by Isaacs to the involvement of lymphatic glands in the disease process. They also often found a type of cell which, apart from these cases, they have seen only in infectious mononucleosis. It occurred in two types, old and young, in 61 per cent of the cases examined and in the infected rabbits. The young cell is $12 \times 13.5\mu$ with an oval or kidney-shaped nucleus, $12 \times 7.5\mu$; its cytoplasm is deeply basophilic and non-granular but curdled. The older cell is $15.0 \times 15.75\mu$ with a nucleus $13.5 \times 9.0\mu$; the intense blueness of its cytoplasm is confined to the edge.

Serum tests

In countries engaged in the present war research on improvements in the technique of serum tests for syphilis have necessarily been practically at a stand-still, but in the United States of America further comparisons have underlined the importance of workers adhering strictly to the instructions of the authors in carrying out serum tests. In the 1940 Critical Survey mention was made of the hope expressed by some workers that, by the use of spirochaetal antigens instead of tissue extracts, the specificity of the serum tests for syphilis would be improved. Recent work by J. A. Kolmer, C. C. Kast, and Elsa R. Lynch (1941) has shown, however, that such antigens are apt to give a high percentage of positive reactions with non-syphilitic sera. With three strains of alleged *S. pallida* the percentages of positive reactions given by 114 non-syphilitic sera ranged from 22.9 to 61.4, and with an antigen made from *S. microdentium* it was 79.4. The reaction with the last-named suggests that complement fixation by non-syphilitic sera with spirochaetal antigens is a group reaction due to antibody evoked by the spirochaetes commonly associated with gingivitis. The position seems to be analogous to the gonococcal fixation reaction, which may be given by sera containing antibodies to *Neisseria catarrhalis* and *Neisseria meningitidis*.

The demand for greater and greater sensitiveness of serum tests for syphilis has stimulated efforts to eliminate non-specific reactivity as much as possible and therefore to extract from the tissue extracts commonly employed in these tests the component responsible for the syphilis reaction uncontaminated by bodies which might react with non-syphilitic reagins. So far, judging by the work of H. Brown and Kolmer (1941), the antigen responsible for the syphilitic reaction is an unknown substance attached in equal proportions to the cephalin and the lecithin fractions of the tissue extract.

Another method of increasing the significance of the reaction between serum and cholesterolized tissue extracts has been evolved by R. J. Kahn, who has shown that in his routine test a positive reaction may be due to one or both of two main types of reagin—syphilitic and what he calls ‘general biologic’—and they are distinguished from one another by the conditions which are optimal to their activity. The syphilitic reaction is intensified at 37°C ., and lessened in intensity at 1°C .; so far as the general biological reaction is concerned the reverse holds good. Kahn proposes, therefore, that in case of doubt the Kahn test should be repeated at 37°C . and 1°C . respectively to settle whether the reaction in question is syphilitic or of the general biological type. In a series of recent papers Kahn, E. B. McDermott, and S. Marcus (1941) have shown that the positive reactions given in the absence of syphilis by the serum of certain animals and in malaria is of the general biological type. They have shown also that the sera of an important proportion of non-syphilitic persons, though they give negative reactions to the standard Kahn test as ordinarily conducted, are positive when it is carried out at 1°C . Donors of such sera may give a positive reaction to the Kahn test when they become febrile. Kahn’s verification test, as he calls it, may perhaps prove to be a means of distinguishing between syphilitic and non-syphilitic leprosy cases, as at present the question is still undecided whether or not leprosy sera give positive reactions in the absence of syphilis. Of 44 leprosy sera reported on by Kahn, McDermott, and Marcus in the papers referred to, 28 gave reactions of the general biologic type and 16 gave syphilitic reactions, but at the time of writing the specificity of the 16 syphilitic reactions had not been determined.

Prognosis

In treating patients with persistently positive reactions the practitioner is often asked about the probable outcome of the disease, seeing that as judged by the serum reactions the treatment seems to be failing to eradicate the parasites. The patient's happiness depends greatly on the confidence with which the reply is given; I have seen very many patients who have been made very miserable by practitioners who, not having taken the trouble to come to a decision on this important subject, have hedged by saying that perhaps this or perhaps that might happen. In cases of persistently positive serum reactions without evidence of organic disease, I commonly say that, if the cerebrospinal fluid is negative and the patient continues treatment, I have no anxiety whatsoever about the outcome. If the spinal fluid has not been tested, I give no opinion but say that, if it should be found positive, the disease can be kept under control. Such a hopeful opinion is made more impressive by citation of the evidence which appears from time to time to show that natural resistance alone often suffices to protect the patient against the effects of *S. pallida* and that positive blood reactions are by no means incompatible with longevity. In a recent paper L. T. Hilliard and B. K. Kirman (1941) report on examinations for syphilis of inmates of the Tooting Bec Hospital, an institution for mentally ill patients over the age of 70. Out of 701 who were examined serologically, 10 per cent had positive Wassermann and Meinicke reactions, or reacted positively to one or the other, and in 64 non-certified cases 8 patients showed abnormal cerebrospinal fluid, 7 with paretic gold curve. The oldest patient in the institution with a positive Wassermann reaction was over one hundred years of age.

Diminution of resistance

The effect of acute syphilis on resistance to infection with other organisms has been tested by M. Fujimori (1940) on animals. He found that during the acute phases of syphilitic infection the antibody response of the animals to injection with different antigens was reduced. In another series of experiments he showed that as the infection proceeded to its climax, the resistance of the infected animals to diphtheria toxin was reduced. These results are interesting in view of the frequent observation that infants with congenital syphilis are more prone than normal babies to die of intercurrent infections.

Treatment

The five-day treatment

Massive arseno-therapy, or the so-called five-day treatment of syphilis, which was mentioned in the Critical Survey for 1940, has naturally attracted keen attention, and already some ways of improving it have been suggested; as can readily be imagined, it appeals to those who are responsible for the care of people who as a class cannot, or will not, persevere with treatment for the many months prescribed in modern schemes. In a symposium of nine papers published in the *Archives of Dermatology and Syphilology* of August 1940 on the pioneer New York experiment on these lines the principle of the five-day treatment was described, the technique and the results with neoarsphenamine and with *m*-amino-*p*-hydroxyphenyl-arsenoxide, which is sold in Great Britain under the trade name 'Marpharside' and in the United States of America and elsewhere as 'Mapharsen'. (For convenience and to avoid confusion in nomenclature in the event of the same compound being marketed under other names this remedy is referred to below as 'arsenoxide'.) In the patients treated with 4 to 5 grammes of neoarsphenamine in 5 days, 13 out of 15 observed for 3 to 5 years were considered to have given satisfactory results, and similarly 91 per cent of 78 others observed for two years. As mentioned in the 1940 Critical Survey, toxic effects with neoarsphenamine had been too frequent, and arsenoxide had been substituted, the total dose of this remedy administered in five days being increased with experience from 400 milligrams to 1,200 milligrams, this dose being given at the rate of 240 milligrams (dissolved in 2,400 cubic centimetres of 5 per cent glucose) a day, or about 3 cubic centimetres per minute. At the time of writing, the results had been analysed in 157 cases which had been treated with total doses less than

1,200 milligrams, and 80 per cent of those who had remained under observation sufficiently long afterwards were considered to have responded satisfactorily. The significance of the fact that in this investigation the results with a total dosage of less than 1,200 milligrams of arsenoxide were not so good as those with a total dosage of 4,000 milligrams of neoarsphenamine is discussed below. The toxic effects observed in the arsenoxide series were much less than in those under neoarsphenamine, and no patient died, but 1 per cent of the cases showed side-effects referable to the central nervous system, a very high proportion when compared with the experience in this respect with ordinary methods of treatment. One great disadvantage of the drip-method of massive arseno-therapy is that the patient must remain for several hours a day in bed with a needle fixed in a vein of one forearm, and to obviate this some workers have tried the effect of frequently repeated injections. H. Gordon (1941) reported on a trial of such a method on negro mine-workers in the Transvaal. After trying a scheme in which 5 injections of 20 milligrams of arsenoxide daily were given on 5 successive days to 84 patients, he doubled the dose, thus giving a total dose of 200 milligrams less than that given by the drip-method in New York. So far as can be judged so shortly after the completion of the treatment, the results of this experiment do not seem to be very impressive, but they may easily be better than those which were being obtained by routine methods of treatment, considering the proneness of negroes to cease attendance for treatment on disappearance of symptoms. E. W. Thomas and G. Wexler (1941) first tried the multiple-dose method, giving eventually two injections of 80 to 90 milligrams daily for 6 days, but had too high a rate of toxic effects and changed over to a combination of multiple doses and fever induced by injections of typhoid vaccine. At the time of writing, it is too early to assess the results fairly, and the method is mentioned here as an indication only of the efforts which workers are now making to shorten the duration of the treatment. Still another development of massive arseno-therapy is that reported by W. M. Simpson, H. W. Kendell, and D. Rose (1941) in which the patient receives 240 milligrams of arsenoxide by the drip-method during 7 hours whilst his temperature is maintained at 106° F. by means of a Kettering Hypertherm. By control series of cases these authors showed that the results of chemotherapy plus pyrexia are better than those with either alone.

Treatment by heat

The controversy on the relative merits of pyrexia by malarial inoculation and by physical agencies such as the Kettering Hypertherm, referred to as artificial pyrexia below, may be mostly settled by the inquiry reported on by P. A. O'Leary, W. L. Bruetsch, F. G. Ebaugh, W. M. Simpson, H. C. Solomon, S. L. Warren, R. A. Vonderlehr, L. J. Usilton, and I. V. Sollins (1940) in which the results in 1,100 cases of general paresis treated with malaria were compared with those in 320 treated by artificial pyrexia. The general conclusion was that in mild and intermediate cases of general paresis the results of the two methods were similar but that in advanced cases artificial pyrexia had the advantage. It has also been shown that artificial pyrexia, being more easily controlled, is applicable to a wider range of cases than is malarial therapy. Simpson's technique at present is to give 12 sessions of 3 hours each at a temperature of 105·8° F.; the sessions may be at the rate of one, two, or even three a week. At the beginning of each an intramuscular injection of bismuth is given, and when the temperature has reached 105° F. the arsenical remedy is injected intravenously; it has been found that patients tolerate arsenical remedies better if these are given during pyrexia. After the above course is completed, the patient is treated for 20 weeks with injections of the arsenical and bismuth preparations used in antisypilitic treatment.

Arsenoxide

In the remarks on the massive arseno-therapy of syphilis above it is mentioned (p. 104) that in the New York service the total dose of arsenoxide has been stepped up to 1,200 milligrams in 5 days, and the quoted percentages

of satisfactory results showed quite clearly that those who had arsenoxide in doses less than 1,200 milligrams in 5 days were significantly fewer than those who had 4,000 milligrams of neoarsphenamine; indeed this fact was stated by B. Webster, one of the contributors to the symposium mentioned above. The relatively inferior results with doses of arsenoxide less than approximately one-third of those of neoarsphenamine are interesting in view of the fact that when arsenoxide is used in routine work its single dose (30 to 60 milligrams for adults) is based on the assumption that it is ten times as potent therapeutically as is neoarsphenamine. That it is not so potent as this is shown by the experience of the New York workers in massive arsenotherapy just quoted, and also by some recently published animal experiments by B. J. Longley, N. M. Clausen, and A. L. Tatum (1941) which were not primarily designed to compare the two remedies but to see if experimental yaws of rabbits would respond as well to antisyphilitic treatment as does experimental syphilis. Incidentally, yaws did so respond, but the important point here is that in this investigation, in which the yaws and the syphilis rabbits respectively were divided into two series, one receiving graduated doses of neoarsphenamine and the other graduated doses of arsenoxide, it is quite clear from the authors' tables that 3.5 milligrams of arsenoxide per kilogram weight of rabbit cured fewer rabbits than did 7 milligrams of neoarsphenamine.

These results are important because they are strong evidence against the view expressed in many clinical reports that, in the dosage commonly employed, arsenoxide is as effective therapeutically as is neoarsphenamine. Reports on results of antisyphilitic treatment of human beings are usually difficult to assess because of the length of observation required and many other factors, including varying resistance to treatment through age of infection and idiosyncrasies; consequently all reports on comparisons of antisyphilitic remedies require very careful scrutiny. This applies with particular force to remedies, such as that under discussion, which promise greater freedom from toxic effects, because with such a 'no-trouble remedy' an element of wishful thinking may blind the observer to evidence of defective therapeutic activity; in forming a judgement of the merits of a remedy from such reports, therefore, the easy path of skipping the evidence and accepting the authors' conclusions is dangerous. Such reports as I have studied on the effects of arsenoxide are by no means convincing that, in the dosage commonly employed, it is therapeutically equal to neoarsphenamine. In most reports the issue is more or less obscured by the fact of the patients having also been treated with mercury or bismuth, but apart from this the published evidence is such as would deter me from substituting arsenoxide for neoarsphenamine in the routine treatment of early syphilis. This statement is made after careful study also of the report by O. H. Foerster, R. L. McIntosh, L. M. Wieder, H. R. Foerster, and G. A. Cooper (1935) on the results of treatment with this remedy alone. The correct assessment of the relative therapeutic value of arsenoxide as compared with that of neoarsphenamine is contained in the experience with massive arsenotherapy and in the animal experiments quoted at the beginning of this discussion. Apparently this view is not shared by the Subcommittee on Venereal Diseases of the Committee on Chemotherapeutic and other Agents of the Committee on Medical Preparedness of the American Medical Association, which recommended arsenoxide as the preferred arsenical for treatment of syphilis in the American Forces. It is interesting to note that under the recommendations of this sub-committee the average patient with early syphilis will receive much less treatment in the first year than does the average British soldier in the same case. The treatment of the latter is on the principles recommended by the League of Nations Committee on the subject, and under it the patient receives in a year approximately 23.2 grammes of neoarsphenamine and 10 grammes of bismuth metal. Under the United States scheme the patient is presumably to receive in the first year 30 injections of bismuth salicylate containing 3.6 grammes of bismuth metal and 24 injections of arsenoxide totalling at most 1.4 grammes; judging by the evidence offered above, 1.4 grammes of arsenoxide are not equal to 14 grammes of neoarsphenamine, so that the treatment provides for administration of

less than half the amount of effective antisyphilitic remedy prescribed for the British soldier.

GONORRHOEA

Diagnosis

Evidence continues to accumulate that cultural methods discover many more gonococcus carriers than does examination of dried films alone; the employment of both methods is better than that of either alone. Hitherto one difficulty in the way of the universal employment of the cultural method has been that it was felt to be useless if there was no incubator on the spot, the mortality of gonococci planted on slopes or plates left in the cold being very high. I have recommended collection and transport of the material in capillary tubes, as the gonococcus remains viable in its native medium for a number of days at room temperature; some years ago E. Mislowitzer (1937) invented a portable incubator in which the heat is supplied by crystallization of a mixture of fatty acids first liquefied by heat, on the same principle as that employed in the recently invented Oxford vaporizers for anaesthetics; but these methods have not acquired much popularity. A simpler method than these, which has been found successful, is to shake the material into 1 or 2 cubic centimetres of an albumen-enriched broth, from which gonococci can be cultivated after it has been for some hours at room temperature. The method of collection from females is important. In adult females G. Sewell, Emilie Clarke, and E. Nelson (1941) recommend that the material be taken up on wool swabs not too tightly rolled and shaken out by twirling the swabs in broth as above. In children, A. Cohn, A. Steer, and E. L. Adler (1940, 1941) recommend that a female catheter which has been dipped in sterile saline be inserted into the vagina. Gillick showed that antiseptic lubricants on specula interfere seriously with culture of gonococci in uterine and vaginal discharges.

Treatment by sulphonamide compounds

In the Critical Survey of 1940 preference was expressed for a short and sharp course of sulphonamide treatment with relatively high doses rather than a long drawn-out one with smaller doses; a recent discussion (1941) on the intensive treatment of gonorrhoea with sulphapyridine, which was held by the Medical Society for the Study of Venereal Diseases, provided strong support for this plan. A. J. King and D. Williams, who opened the discussion, had treated 502 patients with a dosage of 4 grammes at once, 2 grammes at the end of 4 hours, and thereafter 1 gramme every four hours night and day until 72 hours had elapsed from the start of the treatment. The results had been good, but the authors had seen a rather high incidence of haematuria from deposition of sulphapyridine crystals in the kidneys and ureters and had had 2 cases of uraemia, one being fatal. This experience led them to advise that patients undergoing such treatment should be made to take large quantities of fluid, that alkalis should be pushed, that in cases of severe vomiting saline should be given intravenously by the drip-method, and that the total urine should be measured daily with a view to the cessation of the treatment if the amount excreted showed an appreciable diminution. These recommendations were well supported by other speakers in the discussion. R. M. B. MacKenna and R. T. Wordingham had been associated in a trial of intensive sulphapyridine treatment on 3,000 cases with such satisfactory results as to cause them to recommend its adoption whenever practicable. After trial of various plans of dosage they had arrived at one in which 5 grammes was followed at four-hourly intervals day and night by 4, 3, 2, and 1 grammes, the last dose being repeated until a total of 22 grammes had been given in 48 hours. The tablets were given crushed in milk, and 30 grains of potassium citrate or bicarbonate, or sodium bicarbonate, were given every 2 hours. The patient was kept in bed, not allowed to smoke, and encouraged to drink up to 11 or 12 pints of fluid a day.

Sulphathiazole

The intensive treatment of gonorrhoea by sulphonamide compounds is likely to gain in popularity when sulphathiazole becomes more plentiful, as all available evidence indicates that it is as active as sulphapyridine in

gonococcal infections and is undoubtedly more easily tolerated. It cannot be denied that the average patient undergoing intensive treatment with sulphapyridine is very miserable, and there is much to be said for the view that such heavy doses as those mentioned above are mainly applicable to patients in hospital, although, in the discussion mentioned above, Anderson, who was associated with Bowie in the introduction of this method, thought that under it side-effects were less in out-patients. With sulphathiazole J. Gaté and P. Cuilleret (1940) have elaborated a 24-hour cure, the patient taking 2 tablets every 2 hours from 3 p.m. to 11 p.m. on one day and from 6 a.m. to 3 p.m. the next. More remarkable than this is the one-dose cure arrived at by G. Miescher (1940) with the same compound. After starting with a six-day treatment in which the local chemotherapy was supplemented by vaccines and local treatment, he first dropped the local treatment and the vaccines and then began to reduce the duration of the treatment until he arrived at a one-day cure. In this he tried nine different plans of dosage before giving a single dose; this dose varied, but 5 grammes were finally recommended. In a later paper, however, Miescher and A. Schnetz (1941) concluded that, although the one-dose treatment had its uses for certain cases, the best scheme of dosage was 5 doses of 1 gramme each at intervals of 2 hours on each of two successive days. A point of interest brought out by Miescher and Schnetz is that in relapse cases following sulphonamide treatment the gonococci are very slow in growth on artificial media.

Sulphonamides with pyrexial treatment

In cases which have resisted chemotherapy some workers have found that a combination of fever and sulphonamide treatment has proved effective. A. I. Mann (1940), after trying various combinations, recommended 2 days of sulphanilamide, 6.6 grammes daily, followed by 6 hours of fever at 106.5° F. Simpson, Kendell, and Rose have reported on 105 resistant cases treated with artificial fever, either alone or combined with chemotherapy, and concluded that the time-dosage relationship of the chemotherapy to the fever is important; when the drug is administered for 18 hours prior to the fever treatment the effect is much better than when it is given either immediately before or during the latter. Completely satisfactory results were obtained by giving sulphathiazole in 6 doses of 0.5 gramme during 18 hours before an eight-hour fever session at 106° F.

Anuria complicating sulphonamide therapy

The possibility that anuria may be caused by the deposit of crystals of sulphathiazole or sulphapyridine in the kidneys and ureters is a source of anxiety, especially when the treatment is ambulatory, as with most cases of gonorrhoea. The danger seems to be small if the precautions recommended above are taken, but in the event of the development of complete anuria, the prompt washing out of the pelvis of the kidneys, as recommended by J. F. Sadusk, Jun., L. Waters, and D. Wilson (1940), seems to offer the best hope of recovery. (See also p. 117.)

Vulvo-vaginitis of children

Important studies of different aspects of vulvo-vaginitis in children, by Cohn, Steer, and Adler in New York, showed that only 23.3 per cent of the 759 children examined because of suspicion of gonorrhoea infection were gonococcal, a result similar to that reported by the London County Council's Committee on vulvo-vaginitis, and earlier than this by A. C. Ruys (1933), who found gonococci in only 28 of 161 cases of vulvo-vaginitis in children. As regards sources of infection, Cohn and his colleagues were sceptical of lavatory seats, never having traced any case to this source; this scepticism was repeated in their second paper, in which they said that they had never cultivated gonococci from lavatory seats which had been used by children with profuse discharge and that these seats had been used by normal children without untoward result. On the other hand, infected adults in the patients' families, many of them in the chronic stages of the disease, seemed to be the most frequent source of infection, but the authors mentioned also sex conduct with boys under 10 and manipulations under sex curiosity, which

they regard as normal in children, as possible means of transmission. One of the most interesting results of their study was the information which it afforded on the course of gonococcal vulvo-vaginitis when left untreated. The authors left 38 patients without treatment. In 17 the infection cleared up without relapse in from 1 to less than 12 weeks; in another gonococci persisted for 24 weeks before disappearing; in 8 cases the gonococci had finally disappeared by the 16th week after positive specimens had alternated with negative for some time; in a third group, of 12 cases, the patients were reported in the first paper to have become carriers, but in the second, which reported on the results of observation for a further period of 12 weeks, the percentage of spontaneous recoveries was reported to have risen to 78.8. It follows from this that the factor of spontaneous recovery must be taken into account when assessing the value of any form of treatment of this disease; it discounts many of the results of treatment with hormones.

CHANCROID AND GRANULOMA INGUINALE

No work calling for modification of what has been written previously in this publication has appeared during the last year.

LYMPHOGRANULOMA INGUINALE

The relation between lymphogranuloma inguinale and Parinaud's oculoglandular syndrome and trachoma has been discussed at some length by J. P. Macnie (1941) in a paper on 'Ocular Lymphogranuloma Venereum' which shows that the virus of lymphogranuloma may be the cause of conjunctivitis, keratitis, unvitis, and other eye diseases in a higher proportion of cases than may hitherto have been imagined.

Diagnosis

Frei's intracutaneous test is recognized to be one of the most important means of diagnosing lymphogranuloma inguinale, especially in cases of rectal stricture and esthiomène, but reliable antigen is by no means easy to obtain. That made from contents of buboes is irregular in potency, that made from infected brains of mice has the disadvantage that the brain tissue in it may stimulate non-specific reactions, and attention has consequently been turned to the possibility of making antigen from artificial cultures. For this purpose chorio-allantoic membrane of chick embryos has proved disappointing, but G. Rake, C. M. McKee, and M. F. Shaffer (1940) have found that cultivation on the yolk sac of fertile eggs is very successful, and from such cultures they have prepared an antigen, called 'lygranum', which S. E. Sulkin, P. F. Fletcher, E. T. Huber, and E. P. Reh (1941) have reported to be far superior to mouse-brain antigen.

Treatment

Numerous papers have testified to the value of sulphonamide treatment of lymphogranuloma inguinale, and G. M. Findlay (1940) has demonstrated that in mice the administration of *p*-amino-benzoic acid interferes with the action of these remedies in lymphogranuloma inguinale in the same way as it interferes with their action in streptococcal infections. The author says that as lymphogranuloma inguinale and trachoma are the only virus infections influenced by the sulphonamides, it is tempting to suppose that they are the only two requiring *p*-amino-benzoic acid for their metabolism; alternatively that the other viruses make so much of this compound that they are able to inhibit the action of the sulphonamides without help from outside.

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RECENT DEVELOPMENTS IN DRUG THERAPY

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DRUG SHORTAGE AND THE WAR

The shortage of drugs, as a result of the war, has not yet impaired therapeutic efficiency. Nevertheless, in order to conserve shipping and foreign exchange resources, imports of drugs will be restricted to the minimum necessary for home and export purposes; the Ministry of Health urges that scarce drugs should not be prescribed if a satisfactory alternative is available. The Therapeutic Requirements Committee of the Medical Research Council in a memorandum on *Economy in the Use of Drugs in Wartime* (March 1941) has prepared lists of those drugs which are (a) either essential or available, (b) essential for special purposes but to be used with strict economy, and (c) not essential; for categories (b) and (c) available substitutes are indicated. The memorandum rightly points out that although a drug may be unobtainable under a proprietary or branded name it may still be available under its official (B.P., or B.P.C.) name.

Economy in drugs

A Defence Regulation empowers the Minister of Health, after consultation with the Medical Research Council, to make Orders authorizing a chemist to substitute for scarce drugs named alternatives having substantially the same therapeutic action. Such an Order will not apply if the doctor expressly writes against the scarce drug in the prescription the letters 'N.A.' (no alternative) or otherwise indicates that the scarce substance is essential. An Order of this nature has been made authorizing the substitution for potassium bicarbonate, bromide, iodide, and citrate of the corresponding sodium salts in equal quantities.

The strictest economy is necessary in the use of preparations of squill, for which, in the pharmacopoeial preparations, authority (February 28, 1941) is given to substitute Indian squill, and for valerian, Indian valerian may be used. Great care is enjoined in the use of glycerin, and for that in kaolin poultice (cataplasma kaolini) a 70 per cent solution of sodium lactate as substitute is permitted. The prescription of alcoholic preparations should be avoided whenever possible; thus in place of the majority of tinctures, liquid extracts of equivalent efficiency are available and their use will reduce the amount of alcohol consumed.

Pharmacy and Medicines Act

The provisions of the Pharmacy and Medicines Act 1941 which are important for medical practitioners are those requiring the disclosure of the composition of medicines, except in the case of 'any article made up and supplied for the use of a particular person, being an article prescribed by reference to the needs of that person'. Thus the composition of a medical practitioner's prescription or indeed the counter-prescribed preparation of a chemist for the patient need not be stated on the container if it is made up and supplied for the use of a particular person. Apart from this exception, medicines recommended 'in terms which are calculated to lead to the use of the substance for the prevention or treatment of any ailment' may not be sold by retail or sent in sample form unless there is clearly legible on the article or its container (1) the appropriate designation of the substance or of each active constituent or of each ingredient, and (2) in the two latter cases the appropriate quantitative particulars of the constituents or ingredients. The appropriate designation of the substance, active constituents, or ingredients is that of the Poisons List, or, if not a poison, then either that in the *British Pharmacopoeia* or *British Pharmaceutical Codex*, or, if not described in these volumes, the accepted scientific name or other name describing its true nature. The phrase 'appropriate quantitative particulars' means either the approximate percentage or approximate quantity of each constituent or ingredient contained in the substance or the article sold or supplied, or in separate portions thereof.

It should be noted that if the ingredients are disclosed, all must be stated, but if the active constituents are disclosed information on such ingredients as flavours, colouring agents, and solvents may be withheld unless they also have physiological activity.

The Act will be of much value by revealing to the profession the true composition of many proprietary preparations which, under enticing brand names and with an unusual or unaccepted scientific sub-name to disguise their constituents, have been brought by advertisement prominently before the attention of practitioners. The disclosure of the composition of proprietary remedies should also strengthen the ability of the profession to discourage the inappropriate use of these by the public.

FOURTH ADDENDUM TO THE 'BRITISH PHARMACOPOEIA', 1932

The *Fourth Addendum* to the *British Pharmacopoeia*, 1932, became official from October 1, 1941. It was produced for three main reasons: (1) to provide standards for certain articles which have since been included in the *National War Formulary*; (2) to produce in a regularized form monographs of which notice had been given in the official *Gazettes* for February 28, 1941; and (3) to supply amended formulae for a number of pharmacopoeial preparations of which certain ingredients are unobtainable or in very short supply. The following is a brief account of some of the additions to the *Pharmacopoeia*, with short notes on the action and uses of these substances.

New official substances

Mandelic acid and nicotinic acid are now officially recognized substances. The dose of mandelic acid is given as 30 to 60 grains. In actual practice the calcium, magnesium, and ammonium salts of mandelic acid are more commonly prescribed; the acid must be neutralized before administration, 45 grains of the acid requiring 24 grains of sodium bicarbonate. It is necessary to maintain the hydrogen ion concentration of the urine at 5.5, hence ammonium chloride must be given to produce an acid reaction. In the *National War Formulary*, which for National Health Insurance purposes became official on December 1, 1941, mandelic acid is a constituent of a mixture of ammonium mandelate in which 20 minims of strong solution of ammonia are used to neutralize 45 grains of mandelic acid. Although the dose of nicotinic acid is given in the *Addendum* as $\frac{1}{2}$ to $1\frac{1}{2}$ grains, larger doses are administered in pellagra and it is not unusual for as much as $7\frac{1}{2}$ grains to be given in 24 hours (T. D. Spies). It is also used to treat porphyria.

Benzyl benzoate

Benzyl benzoate is added to the *Pharmacopoeia*, presumably because of its value in the treatment of scabies (see p. 120). A dose of 5 to 8 minims is recommended in the *Addendum*, and thus it may be assumed that the Pharmacopoeia Commission have produced a standard specification in order that the purity of the drug for administration in spasmodic asthma and intestinal colic may also be assured. In the new Supplement to the *British Pharmaceutical Codex*, published in November, 1941, there is a 25 per cent emulsion of benzyl benzoate in which the drug is suspended by the aid of triethanolamine stearate, and also a clear lotion of benzyl benzoate, in which a medium of spirit soap and alcohol is used.

Substances of German origin

Two chemicals are included in the *Addendum* in order to provide standards for substances which are primarily of German origin and which British chemical manufacturers are now able to supply. They are: pamaquin, the British equivalent of the malarial specific plasmoquine, and suramin, the equivalent of Bayer 205, used in 10 per cent solution for the prophylaxis and treatment of trypanosomiasis.

Injections

There are five new pharmacopoeial injections, those of (1) calcium gluconate, a supersaturated solution of the salt used to arrest inaccessible haemorrhage and to check tetany; (2) nikethamide, the equivalent of coramine; (3) procaine and adrenaline, a useful local anaesthetic for dental and minor operations; (4) quinine and urethane, and (5) sodium morrhuate, the last two being solutions used as sclerosing agents for varicose veins.

Additional monographs

Other substances, new to the *Pharmacopoeia*, for which modern practice has made it desirable to provide standards of purity, include bismuth subgallate, formerly known as the German proprietary dermatol; digoxin, the crystalline glycoside from

Digitalis lanata; ephedrine, the hemi-hydrate of the alkaloid from ephedra, used to relieve catarrh in hay fever and other nasal infections; magnesium trisilicate, a valuable antacid for hyperchlorhydria and peptic ulcer; morphine sulphate, one of the most soluble and stable salts of morphine; light liquid paraffin, the vehicle for oily nasal sprays; phenylmercuric nitrate, a potent bactericide now authorized to be used as a preservative in parenteral injections; proflavine sulphate, one of the most effective antiseptics of the acridine dye series; and sulphanilamide, the sulphonamide which in the interests of economy should be prescribed whenever possible, to the exclusion of the more expensive sulphapyridine, sulphathiazole, sulphadiazine, and sulphanilylguanidine.

Sterilization methods

Tyndallization has been withdrawn as a means of sterilizing solutions intended for injection, and instead, sterilization is effected by adding to the solution or preparation chlorocresol (0.2 per cent w/v) or phenylmercuric nitrate (0.002 per cent w/v) as a bactericide, and maintaining the solution at 98° to 100° C. for thirty minutes. The *Fourth Addendum* and the *Codex Supplement* give in tabular form new directions for the methods by which solutions of drugs to be administered by injection should be sterilized.

Names of proprietary drugs

Recently, the General Medical Council approved names for drugs formerly supplied under proprietary names and now to be produced by British firms. In the following list, the official name which should be used in prescriptions is given first, followed in brackets by the proprietary or chemical names:

Amethocaine Hydrochloride (decicain, pantocaine); *Menaphthone* (2-methyl-1:4-naphthoquinone) representing vitamin K, the coagulation vitamin, which increases the prothrombin content of the blood; *Pethidine Hydrochloride* (dolantin, dolantal, 1-methyl-4-phenyl-piperidine carboxylic acid ethyl ester); *Soluble Phenytoin* (epanutin, eptoin, solantoin, soluble dilantin, sodium diphenylhydantoinate) and *Sulphacetamide* (albucid) or *p*-aminobenzene-sulphonacetamide, a soluble and neutral sulphonamide.

HEALING OF WOUNDS

In the physiological healing of wounds differences exist in the processes of repair. In a small wound migration of both epithelial and connective tissue cells suffices, while compensatory mitosis occurs, after healing, only around the fringes of the wound. A large wound becomes temporarily filled with granulation tissue—composed of blood vessels and young connective tissue—and, in the case of the covering epithelium, cell migration has to be supplemented by cell division, which becomes more important in larger wounds.

It has been shown that cellular mitosis depends upon the presence of the sulphydryl (—SH) radical and that wound repair by mitosis depends on the restoration of the disturbed balance between sulphydryl (—SH) and sulfoxide (=SO) groups, i.e. the sulphydryl groups formed by denaturation of proteins from injured cells excite mitosis, whereas the sulfoxide groups, into which the sulphydryl groups are rapidly converted, arrest the action of the sulphydryl groups. On this principle clinical trials have been made of sulphydryl compounds. Glutathione has proved active but is expensive. Good results in wounds, burns, and indolent ulcers have been obtained with a 1 : 10,000 solution of *p*-thiocresol and a 0.5 per cent ointment of thiocresol in lanolin. Cystine as a fresh 0.5 per cent solution, buffered by alkaline phosphate, in equal parts of distilled water and saline, is also effective, and an ointment of cystine (0.5 per cent in lanolin) has caused a 30 to 40 per cent acceleration of healing in large excised wounds. Favourable results are also recorded in burns, scalds, and decubitus ulcers (J. F. Riley). Further clinical trials will determine if these advantageous results are constant. (See also pp. 13 and 121.)

TREATMENT OF BURNS

Opinions upon the ideal treatment for burns have undergone rapid changes but without establishing a technique which meets with general approval. The use of tannic acid (5 per cent) as a coagulant is regarded as the cause of impaired function and gangrene associated with second and third degree burns of the hands. Criticism has also been directed against the silver nitrate (10 per cent) and tannic acid technique.

Nevertheless, in the past both these methods did eliminate toxæmia and sepsis and lowered mortality. Recently D. M. Glover and A. F. Sydow recommended that between the fifth and eighth day, when the coagulum begins to separate, continuous dressings with Dakin's solution should be applied so that the wound becomes a granulating surface suitable for skin grafting.

Instead of applying tannic acid in such cases, saline compresses or intermittent saline baths have been recommended as treatment for a week or until oedema and sepsis have been eliminated; afterwards if coagulation methods are thought advisable, treatment with gentian violet or triple dye—gentian violet (0.25 per cent), brilliant green (0.25 per cent), and euflavine (0.1 per cent)—may be applied to form a partial casing, e.g. to the backs and fronts but not to the sides of the fingers (S. M. Cohen; E.M.S. Memo. Gen. 325). (See also p. 11.)

Bunyan-Stannard envelope

Lately the advantages of the Bunyan-Stannard envelopes of a coated silk fabric in providing a means for the frequent irrigation of burns and wounds have been emphasized; the envelopes are watertight, flexible, transparent for observation, and designed to fit any limb. The area within the envelope is irrigated for from 10 to 20 minutes twice or thrice daily with a non-toxic antiseptic at a temperature of 100° F.; a 1 per cent electrolytic sodium hypochlorite solution (E.S.H.) forms the stock solution; it is less alkaline and irritating than Dakin's solution. It is used in dilutions of from 5 per cent (i.e. 0.05 per cent sodium hypochlorite) to 50 per cent in water, depending on the condition of the burnt or wounded surface, the higher concentrations being employed to cleanse burns containing dead tissue. After the irrigations have been carried out, the envelope is drained and inflated with oxygen. It is claimed for this method that, even without surgical cleansing, it prevents other than mild infections and is successful in the early preparation of an area suitable for skin grafting. As first-aid treatment for burns, J. Bunyan recommends that packs soaked in electrolytic sodium hypochlorite solution should be applied to relieve pain, to prevent fluid loss, and to act as initial antiseptics (Bunyan; R. V. Hudson; R. S. B. Pearson, E. E. Lewis, and R. B. Niven; J. W. Hannay).

First aid for burns

A recent (1941) memorandum to Emergency Medical Services officers advises as first aid for minor burns, after cleansing with soap and water, application to the hands and face of sterile gauze treated with soft paraffin, and to other parts tannic acid or gentian violet jelly, 1 per cent, and no dressing. Serious burns should be covered with the sterile soft paraffin gauze and the patients sent to hospital. At hospitals, serious burns should be cleansed, lightly dusted with sulphanilamide powder and a coagulant solution applied, except in cases in which the face, hands, wrists, or feet are affected; in areas which should not be tanned, the burn is dusted with sulphanilamide powder, a sterile *tulle gras* dressing applied, and warm saline gauze dressings applied frequently.

THE SULPHONAMIDES

Used locally as wound antiseptics

Sulphonamides inhibit the growth of haemolytic streptococci in dilutions of 1 : 25,000 or less; they are not, however, active bactericides, but enable the leucocytes to kill the bacteria because sulphonamides are not toxic to leucocytes until strengths of about 1 : 200 are reached. The local antiseptic action of all sulphonamides is greatly reduced (1) if application be delayed beyond two hours after the wound is received, (2) by the presence in the wound of large numbers of living or dead bacteria, purulent fluid, or peptone.

Sulphathiazole is the most potent antiseptic of the three, and against haemolytic streptococci sulphapyridine is about ten times more powerful than sulphanilamide, which, on the other hand, is better than sulphapyridine against *Clostridium welchii* but less so against *Clostridium septique*. All have locally only a slight inhibitory influence on *Clostridium oedematiens*. Sulphathiazole is most effective against staphylococci and in a strength of 1 : 60,000 inhibits their growth.

The relative solubility in wound fluids and the absorbability of sulphonamides are important. Sulphanilamide is the most soluble and is absorbed within 24 hours, thus it gives a brief but high concentration of from 1 to 1.5 per cent in wound fluids.

Sulphapyridine is less soluble (0.1 per cent) and is absorbed very slowly in 7 to 10 days. Sulphathiazole is least soluble (0.05 per cent) but is absorbed in 5 to 6 days, hence although the last is the most potent as an antiseptic, its low solubility and diffusibility reduce its local efficiency (A. Fleming¹; L. Colebrook and A. E. Francis; L. G. Goodwin and G. M. Findlay; F. Hawking¹). Sulphanilylguanidine, which is fairly soluble, is removed from wounds rapidly, but sulphadiazine, less soluble than sulphathiazole, is absorbed slowly (Hawking²).

In concentrations from saturation downwards and for periods between 14 and 72 hours tests of sulphonamide toxicity upon tissue cultures of fibroblasts, macrophages, and epithelial cells show that although sulphathiazole is the most toxic to tissue cells the effective toxicity of these drugs under clinical conditions depends on their relative solubility and is in descending order of potency as follows: sulphanilamide, sulphathiazole, sulphapyridine, and sulphadiazine. Tissue culture experiments prove that for direct application to wounds their relative effects on tissues can be disregarded in favour of their specific bactericidal powers (F. Jacoby, P. B. Medawar, and P. N. Willmer).

When sulphanilamide or sulphathiazole up to an amount of 5 grammes (75 grains) has been inserted into wounds, suppurating sinuses, or varicose ulcers, the concentration of sulphonamide in the blood after 24 hours is found rarely to exceed 1.5 milligrams per 100 cubic centimetres and usually it is 0.5 milligram or less, therefore local treatment can safely be reinforced by oral administration (Hawking³). (See also p. 10.)

Technique.—In view of the reduction in the efficacy of sulphonamides by bacteria and purulent fluid, wounds should be subjected to thorough surgical cleansing or excision and then they should be dusted or insufflated over every surface with sulphanilamide or sulphathiazole powder in amount from 5 grammes (75 grains) to 20 grammes (300 grains), or with a mixture of sulphanilamide 2 parts and sulphathiazole 1 part. Wounds treated with sulphonamides heal with unusual rapidity and often by first intention. If the wound be large, and suturing at first impracticable, it should be packed also with sterile soft paraffin gauze impregnated with sulphanilamide powder and drawn together with elastoplast; usually it can be left for 5 days, when, if found clean, secondary suturing is often possible. Although the sulphonamides have a relatively small inhibitory influence on gas-gangrene organisms, wounds so infected should be treated locally with sulphathiazole, which is the most effective against *Clostridium septicum* and *Clostridium oedematiens*, or with sulphanilamide; but, in addition, the patient should be given the appropriate antiserum. In recent experiments with sulphanilylguanidine and sulphadiazine on wounds infected with *Clostridium welchii* and *Clostridium septicum*, it was concluded that sulphanilylguanidine is markedly inferior to, while sulphadiazine is no better than, sulphathiazole in protecting animals against these organisms (Hawking³).

Ointments.—Ointments and non-greasy creams containing 5 per cent sulphanilamide are on trial as local antiseptic applications; satisfactory results have been reported but their sphere of utility has yet to be determined. Experiments with 30 per cent sulphanilamide in simple ointment produced no local bacteriostatic action, but the diameter of the circular area of stasis caused by the same strength in liquid paraffin was 3.9 centimetres, in olive oil 4.0 centimetres, and in glycerin 4.5 centimetres; or with the powder alone 4.0 centimetres. The local activity of sulphanilamide is thus greatest when dispersed in glycerin (A. M. Locatelli and S. Bowden). Recently a sulphanilamide ointment prepared with sodium alginate has been recommended; it is neither irritating nor greasy and is suitable for application to wounds and to the conjunctiva (*J. Amer. med. Ass.* (1941) 116, 356 and 1336; *Brit. med. J.* (1941) 2, 92; *Pharm. J.* (1941) 1, 251).

Used internally in septicaemias

Pharmacology.—(a) Cyanosis. It has been recognized that the cyanosis resulting from sulphonamides is not related to the formation of methaemoglobin or sulphaemoglobin. Recent investigations have shown that sulphanilamide and sulphapyridine, when oxidized, form pigments which, absorbed upon the fatty envelope of the erythrocytes, produce effects similar to those seen in cyanosed patients. A blue oxidation product (becoming brown on reduction) can be formed by aerobic ultra-violet radiation of dilute aqueous solutions of sulphanilamide. It may be that in the blood the blue oxidation product can oxidize haemoglobin to methaemoglobin and thus become

itself reduced, but its reduction is reversible. Many oxidation products of sulphonamides have been isolated from the urine, some, e.g. *p*-aminophenol, are known to cause methaemoglobinaemia and also porphyrinuria; they may ultimately afford an explanation for other toxic effects of the sulphonamide group (G. V. James¹; C. L. Fox, Jun., and J. E. Cline).

(b) Excretion. Sulphonamides are excreted partly in conjugated form as acetyl compounds; in patients under treatment the CO₂-combining power of the blood and its percentage of glucose is reduced; the use of these sources to form the acetyl radical can be obviated, and thus the toxicity of sulphonamides lowered, by the administration of sodium bicarbonate or, better, of sodium lactate or acetate, as precursors of the acetyl radical. Acetates also make the urine alkaline, which in some infections enhances the bactericidal powers of sulphanilamide in the urine; but their administration with sulphapyridine may lead to increased precipitation of the needle-like crystals of acetylsulphapyridine, which cause haematuria (H. Southworth; James²). (See also p. 6.)

Relative toxic effects of sulphonamides.—Considering the large number of patients who, during some four years, have been treated with sulphonamides, reports of toxic effects have been surprisingly few and rarely of a serious character. Increased experience shows that nausea and vomiting are most frequent from sulphapyridine, fairly common with sulphanilamide, and uncommon from sulphathiazole; conversely, skin rashes arise in 5 per cent of sulphathiazole cases but in only 2 per cent of patients treated with sulphapyridine or sulphanilamide. Haematuria, resulting from crystallization of the needle-like acetyl derivatives within the kidney, is almost unknown from sulphanilamide, whereas it occurs from sulphapyridine in 8 per cent and from sulphathiazole in 2.5 per cent of cases. The serious reactions of acute haemolytic anaemia, which may occur early in treatment, and of agranulocytosis, which does not usually arise until after 14 days' treatment or after 25 grammes (375 grains) have been given, seem to be most frequent from sulphanilamide; but, assuming that one million patients—a low estimate—have been treated with sulphanilamide, the reported incidence of cases of both complications would work out at 0.007 per cent, a negligible risk (P. H. Long, J. W. Haviland, Lydia B. Edwards, and Eleanor A. Bliss; J. A. Kolmer).

The haematuria and renal colic, arising from sulphapyridine especially, usually subside within 24 to 48 hours if the drug be withheld; the condition can be avoided or treated by free administration of fluids. Nitrogen retention and anuria are rare, the latter seldom lasting more than 24 hours; in both conditions improvement has followed the intravenous injection by the drip method of 4.28 per cent sodium sulphate solution with 5 to 10 per cent glucose in physiological saline (J. C. Leedham-Green; J. R. Hughes). (See also p. 6.)

Clinical applications

Sulphathiazole.—Last year's uncertainty about the therapeutic position of this drug has been rectified by increased clinical experience. In lobar pneumonia sulphathiazole is certainly less apt to cause nausea and vomiting, but it is more likely to cause dermatitis and lowers the temperature more slowly than sulphapyridine (W. F. Gaisford and W. Whitelaw; P. H. Long, 1940; J. G. Reinhold, H. F. Flippin, and L. Schwartz; W. W. Spink and A. E. Hansen). As a curative agent it is not more efficient than sulphapyridine, although in type II and VII infections it gives better results. Sulphathiazole does not gain access to the cerebrospinal fluid so satisfactorily, its concentration there being only one-third as compared with sulphapyridine and sulphanilamide, two-thirds that of the blood. It appears to be a more effective bactericide than the other two in infections by the following organisms: *Streptococcus faecalis*, *B. coli*, *B. proteus*, and *B. aerogenes*, *Cl. welchii*, *septicus* and *oedematis*, and the salmonella group; for *Streptococcus viridans* infections it has been proved approximately equal to sulphapyridine. Septicaemias and local diseases, e.g. osteomyelitis and carbuncles, due to *Staphylococcus aureus*, respond as a rule better to treatment with sulphathiazole, but the results so far gained have not substantiated the anticipation that sulphathiazole would prove a specific against staphylococcal infections; it should, however, be the drug of primary choice. Sulphathiazole, like sulphanilamide, acts most efficiently in the majority of urinary infections at a hydrogen ion concentration of 7.5; lower values than this require higher concentrations of both drugs. Weak concentrations of sulphathiazole (25 milligrams per 100 cubic centimetres of urine) suffice to

control some forms of *B. coli* infection but others require more. The toxicity of sulphathiazole towards bacterial invaders of the urinary tract is in descending order as follows: *Staphylococcus aureus*, *B. proteus*, *B. aerogenes*, *B. coli*, *Streptococcus faecalis*, and *Ps. pyocyanea* (H. F. Helmholz). Its efficiency in gonorrhoea equals that of sulphapyridine (H. B. Jones and R. W. Fairbrother; V. E. Lloyd and D. Erskine). Acetylsulphathiazole is about twice as soluble in alkaline urine; hence alkalis or citrates are useful with an increased fluid intake to obviate deposition of its crystals.

Under the name cibazol, or Ciba 3714, sulphathiazole has been used recently in Switzerland as an instillation for potentially infected wounds in amounts from 0.3 (5 grains) to 3.8 grammes (57 grains); most of the wounds healed by first intention without untoward effects; bacteriological tests indicated that the powder was bactericidal. The local application of flexible pencils, containing 10 per cent, was followed by improvement in some cases of cervical endometritis and a 5 per cent ointment was found valuable in impetigo. Oral dosage, intramuscular and intravenous injections are reported to be well tolerated (Annotation (1941) *Lancet*, 2, 46). (See also p. 6.)

Sulphamethylthiazole is akin to sulphathiazole, in that it is relatively insoluble in water, although its sodium compound is soluble. It does not appear to be any more effective against staphylococci, but successful treatment by it has been recorded in septicaemia due to *Staphylococcus aureus* and in urinary infections from this organism, *B. (E.) coli*, and *Streptococcus faecalis* (T. L. Pool and E. N. Cook). In gonorrhoea its potency is about equivalent to, but slower than, that of sulphathiazole (J. Gaté and P. Cuilleret; Lloyd and Erskine).

Sulphonamides as urinary antiseptics

The relative values of the sulphonamides in bacterial infections of the urinary tract are now capable of more accurate definition. *B. coli* infections can be satisfactorily treated by either sulphanilamide or mandelic acid. *Streptococcus faecalis* yields to mandelic acid therapy but is uninfluenced by sulphanilamide, yet sulphathiazole has been shown to be toxic to this organism, particularly if the urine be acidified to a hydrogen ion concentration of 5.5. Conversely, *B. proteus* infections are successfully eliminated by sulphanilamide acting in an alkaline urine; in this infection ammonium chloride does not acidify the urine sufficiently to render mandelic acid effective.

Gonorrhoea

Sulphapyridine is the drug of choice and has been shown to be superior to uleron therapy except in the treatment of chronic gonorrhoea in women. It is generally agreed that sulphapyridine therapy should be accompanied by urethral irrigation with 1 in 8,000 solution of potassium permanganate or mercuric oxycyanide in order to clear gonococci from urethral crypts. Various methods of dosage have been advocated: 1 gramme 3 times daily for 7 or 10 days is common. The routine Army method is that of Osmond, namely first day on diagnosis, 2 grammes (30 grains) of sulphapyridine and 0.5 gramme (8 grains) every 4 hours and 2 grammes (30 grains) at bedtime; second day, a total of 4 grammes (60 grains); third to seventh day, 3 grammes (45 grains) of the drug daily. Others advise, along with daily irrigations, 0.5 gramme (8 grains) sulphapyridine thrice daily during the first week and 0.25 gramme (4 grains) thrice daily during the second week, and irrigation alone during the third week (D. J. Mackinnon), or 0.5 gramme (8 grains) 4 times a day for a week with irrigation continuing for 2 or 3 weeks after (J. Sommerville).

R. M. B. MacKenna and R. T. Wordingham emphasize that early dosage should be maximal, advise maintenance of dosage during the night, a milk diet and liberal barley water during treatment, and the avoidance, by the use of cascara sagrada, of constipation. Smoking increases the liability to nausea and vomiting, and sodium citrate, 2 grammes (30 grains) 2-hourly, in solution, is beneficial. In 48 hours they give 22 grammes (330 grains) of sulphapyridine, the tablets being crushed and given in milk every 4 hours during the day and night; the initial dose, 5 grammes (75 grains); second, 4 grammes (60 grains); third, 3 grammes (45 grains); fourth, 2 grammes (30 grains); and the remaining 8 doses are each 1 gramme (15 grains). Headache, lassitude, nausea, and vomiting may result; lumbo-costal pain and deep tenderness in the upper lumbar regions, followed by haematuria, occurred in some cases, but the urinary symptoms subsided in 48 to 60 hours and no permanent damage was done to the kidneys. Cure and return to duty is usually effected within 8 to 10 days but the patient is kept under observation for 3 months. (See also p. 107.)

Sulphonamides in other infections

The sulphonamide drugs have been used in many different infections, often purely empirically or experimentally, and without bacteriological identification of the infecting organism. In view of the known variations in their relative potency as bacteriostatic agents for different organisms, it is important for success that the appropriate sulphonamide should be employed. The following notes represent some of the numerous conditions in which therapeutic advantages have been gained within the past year.

Lupus erythematosus.—Early cases of lupus erythematosus which improved with treatment by sulphanilamide and sulphapyridine are believed to be of streptococcal origin. A characteristic reaction, appearing in 8 to 10 days, consists of fever, focal reaction in the patches, and muscular pains; it is followed by lessening of the eruption. Such reactions do not occur, nor is the eruption improved, in tuberculous infections (H. W. Barber; F. Glyn-Hughes and A. M. Spence).

Bacillary dysentery.—The bacteriological freedom of cases of Flexner bacillary dysentery has been achieved by the fifth day following daily oral administration of sulphapyridine. The temperature became normal within 24 to 48 hours, the stools, with diminishing blood and mucus, became normal about the fifth day, and the general condition rapidly improved so that patients could get up on the seventh day (W. G. Masefield; G. J. Bell). (See also pp. 6 and 64.)

Bacterial endocarditis.—The value of the anticoagulant, heparin, in subacute bacterial endocarditis, as a means of preventing the deposition of thrombi on the endocardium and valves, in association with sulphapyridine, has not proved uniform. It was anticipated that the heparin would facilitate exposure of the bacteria to the action of sulphapyridine, but an analysis of the cases reported does not substantiate these expectations. Prolonged dosage for 3 or 4 months with sulphapyridine—or sulphathiazole which, although it is weak, has an influence on *Streptococcus viridans*—appears at present to be the most hopeful line of treatment (J. G. MacLeod; G. C. Dockera and E. Kaweran; S. Sevt; C. M. Fletcher). (See also p. 12.)

Ocular infections.—Sulphanilamide penetrates into the ocular fluids and tissues in efficient concentrations if given orally and at least to the anterior chamber if applied locally. In hypopyon corneal ulcer, commonly pneumococcal, subconjunctival injections (5 minims), in two or three depots, of soluseptasine (10 per cent) or sulphapyridine (0.07 per cent) should be given and, when the organism is determined, the appropriate sulphonamide is also given orally. Sulphapyridine, finely powdered and preceded by a local anaesthetic, is dusted over the cornea thrice daily in pneumococcal infections; for streptococcus, sulphanilamide powder or soluseptasine drops are used; and for staphylococcus, sulphathiazole as drops of a 0.1 per cent solution in 1.4 per cent saline (I. L. Johnstone). Early treatment of trachoma with sulphanilamide orally and drops locally of a soluble sulphonamide affords prompt relief from pain and photophobia, improves the condition, and lessens the risk of blindness. Albucid, *p*-aminobenzenesulphonacetamide, is recommended in 2.5 per cent solution as drops every 6 hours in cases of eye lesions from mustard gas or lewisite; it is issued in ampoule form (5 cubic centimetres of a 30 per cent solution).

Aural infections.—In acute otitis media, bacteriological examination, if possible, should determine the selection of the specific drug, and it should be realized that these drugs are unlikely to be beneficial in the presence of undrained pus or an infected venous thrombus. Early treatment with sulphonamides of acute otitis media curtails the duration of the discharge and obviates mastoid operations in a high proportion of cases. The primary infection is usually streptococcal, less frequently pneumococcal, but secondary infection from *Staphylococcus aureus* and *albus*, *B. coli*, *B. proteus*, and *B. pyocyaneus* are common. Paracentesis should be performed when necessary, and adequate doses of the sulphonamides used and maintained for three days after clinical symptoms have disappeared (Annotation (1941) *Brit. med. J.*, 2, 20). (See also p. 56.)

Other diseases.—Successes have also been recorded in the treatment of actinomycosis (G. C. Dorling and N. L. Eckhoff; J. H. Stanyon; W. H. Ogilvie); from sulphapyridine in glandular fever (H. S. Stannus and G. M. Findlay) and in the elimination of meningococci from the nasopharynx of carriers (R. W. Fairbrother); from sulphathiazole without operation in an infant suffering from osteomyelitis complicated by pericarditis (D. H. Patterson and A. J. Walker), and from sulphapyridine with hexobarbitone soluble (evipan sodium) in tetanus (J. Bryant and H. D. Fairman).

New compounds

Sulphadiazine (2-sulphanilamido-pyrimidine).—Sulphadiazine is less soluble in water than is sulphapyridine, but more soluble in blood plasma in which it reaches higher and longer sustained concentrations, hence it may be given at 6-hourly intervals. It is also less toxic and does not cause nausea or vomiting. Sulphadiazine attains a concentration of two-thirds that of the blood in the cerebrospinal fluid. The conjugated compound, acetylsulphadiazine, is formed to a slight extent only and is more soluble in urine and therefore easily excreted. Sulphadiazine appears to be equal to other sulphonamides in the treatment of streptococcal, pneumococcal, and staphylococcal infections and to be superior in attacking *B. Friedländer* and *Cl. welchii*. (W. H. Feinstone; W. H. Feinstone, R. D. Williams, R. T. Wolff, Evelyn Huntington, and M. L. Crossley; O. L. Peterson, E. Strauss, F. H. L. Taylor, and M. Finland; P. H. Long). (See also p. 6.)

Sulphanilylguanidine.—This appears to be too slowly absorbed to be of value in general infections. By oral administration, 0.05 gramme is given per kilogram body weight. It may, however, prove useful in intestinal infections and has given promise of utility in treating bacillary dysentery. Its local application to wounds infected with *Cl. welchii* and *Cl. septicum* has proved inferior to the effect of sulphathiazole (E. K. Marshall, Jun., A. C. Bratton, Lydia B. Edwards, and Ethel Walker; Annotation (1941) *Lancet*, 1, 388).

Promin (p.p'-diamino-diphenyl-sulphone-N.N'-dextrose-sulphonate).—This compound, given intravenously in 5-gramme (75 grains) doses thrice daily, is on trial in the treatment of tuberculous infections (J. A. Toomey; W. H. Feldman, H. C. Hinshaw, and H. E. Moses).

Penicillin.—This substance of unknown composition is formed during the growth of the mould *Penicillium notatum*. It is a powerful bacteriostatic agent even in its impure state, which is a brown powder, freely soluble in water. Recent work has determined the conditions for gaining a good yield of penicillin, namely, a fluid glucose medium, containing sodium nitrate with potassium dihydrogen phosphate, potassium chloride, magnesium and ferrous sulphates, kept at a temperature of 24° C. and at a hydrogen ion concentration of about 7. The culture medium, in which the *Penicillium notatum* is grown, should not be deeper than 2 centimetres. In order to obtain the penicillin, the culture medium is drawn off from beneath the mycelium and, with aseptic precautions, is replaced by fresh medium in which more penicillin forms, and more rapidly than at first. Penicillin is extracted from aqueous solutions adjusted to pH₂ rapidly (because at this hydrogen ion concentration it is unstable) by means of ether or amyl acetate, and is re-extracted by shaking with phosphate buffer or with water at a hydrogen ion concentration of 6–7. A pyrogenic substance, present in this crude extract, is removed by treatment with charcoal, ether extraction, alumina, and the like; finally, a non-pyrogenic reddish-orange fluid 'therapeutic or purified penicillin' is obtained. This is stable if saturated with ether and stored in a refrigerator, or it can be dried to form a brown powder which, since it is hygroscopic, must be kept in a desiccator. A watery solution of the sodium salt is stable in the ice-chest. Instructions for large-scale production suggest that supplies may soon be available, but the use of penicillin may have to be confined to cases which fail to respond to sulphonamides.

The 'assay value' of a penicillin solution is determined for *Staphylococcus aureus* on agar plates from the diameter in millimetres of its zone of inhibition around implanted open tubes of uniform size containing the penicillin solution. An arbitrary unit for comparison has been selected; 'purified penicillin' contains 40–50 of such units per milligram.

Actions of penicillin.—Penicillin is powerfully bacteriostatic but not bactericidal. Dilutions of from 1 in 2,000,000 to 1 in 1,000 inhibit growth of most pathogenic organisms *in vitro* and the detailed table in the original article shows its highest efficiency to be upon the gonococcus, meningococcus, *Staphylococcus aureus*, *Streptococcus pyogenes*, *B. anthracis*, *Cl. tetani*, *Cl. welchii*, and *Streptococcus viridans*, although variations occur in the susceptibility of different strains of bacteria to its action. The bacteriostatic power, unlike that of the sulphonamides, is not influenced by the numbers of bacteria present, nor by products of tissue autolysis or pus—factors of importance in the treatment of suppurating wounds. Penicillin has a low toxicity to cells: dilutions of 1 in 500 do not influence leucocytic activity *in vitro*, although

dilutions of 1 in 1,000,000 are bacteriostatic to streptococci and staphylococci; tissue culture experiments show its minimal lethal concentrations for fibroblasts to be 1 in 1,600, and for epithelial cells and hen's macrophages 1 in 2,000.

Therapeutic trials of penicillin.—Given intravenously in man, a dose of 200 milligrams (3 grains) had not any toxic effect and blood samples from the case still possessed slight bacteriostatic effect after 2 hours, and urinary excretion continued for at least 6 hours. Penicillin is also absorbed if injected subcutaneously or intramuscularly. As it loses activity rapidly in an acid medium, oral administration of penicillin presents difficulties; it has been given successfully by duodenal tube to man and along with sodium bicarbonate to a baby; administration in salol coated capsules or by the rectum is less successful. Excretion of about half the penicillin occurs in the urine, which becomes bright yellow and acquires antibacterial activity; from the urine penicillin can be recovered and used again; a proportion appears to be excreted in the bile.

The results of early therapeutic trials show that with intravenous dosage of 100 milligrams ($1\frac{1}{2}$ grains) every 3 or 4 hours no toxic effects result from a total amount of 4.4 grammes (66 grains) in 5 days. A few severe cases, most resistant to sulphonamide therapy, of staphylococcal and streptococcal septicaemia, carbuncle and cavernous sinus thrombosis (*Staphylococcus aureus*) have been treated with remarkable temporary improvement including fall in temperature with relief of pain and inflammation. In an infant of 6 months, oral dosage (20 milligrams) with 2 grammes of sodium bicarbonate at 1- to 3-hourly intervals cured a staphylococcal infection of the urine. Local application on the conjunctiva of 1 in 5,000 to 1 in 500 solutions of penicillin in physiological saline at hourly intervals is not irritant and has cured conjunctival infections (E. P. Abraham, E. Chain, C. M. Fletcher, H. W. Florey, A. D. Gardner, N. G. Heatley, and M. A. Jennings). (See also p. 6.)

TREATMENT OF SKIN DISEASES

Scabies

Much difference of opinion has been expressed lately upon the ideal method of treating scabies. Sulphur ointment and sulphide or sulphite lotions are well known to provoke dermatitis. The following alternatives to sulphur therapy are recommended, the patient having had the usual bath and scrub. Mitigal, dimethyl-diphenylene-disulphide, as an ointment has given very good results when applied to the affected areas for three successive evenings. Benzyl benzoate, industrial methylated spirit, and soft soap, equal parts, or benzyl benzoate 33, stearic acid 2.5, triethanolamine 0.5 in water to 100, or 'proscabin' are emulsions also regarded as superior in efficiency to sulphur treatment and are free from irritant properties (F. A. E. Silcock; R. E. King; R. W. Carslaw¹; Carslaw²). An improved formula is given in the Supplement to the B.P.C.—benzyl benzoate 2.5, spirit soap 1.5, industrial methylated spirit to 10. Latterly rotenone, the active principle of derris root has been advocated in 1 or 2 per cent strength in lotions or ointments (S. Caller; L. Saunders). Derris root in fine powder 4 oz., soap flakes $3\frac{1}{2}$ oz., and cold water 1 gallon, form an emulsion which is much cheaper although effective (Saunders; J. F. Buchan). It should be noted that mitigal is now difficult to obtain.

Impetigo

Recently a paste of brilliant green stearate has given highly satisfactory results in the treatment of impetigo (Carslaw); and, after removal of scabs, application three times daily of an ointment of 5 per cent sulphathiazole in yellow soft paraffin is stated to cause improvement in 48 hours and healing by the fifth day (A. J. Steigman).

THE VITAMINS

The detailed account given of the vitamins in the 1940 Supplement may be briefly brought up to date. (See also pp. 5 and 49.)

Vitamin A

It has been shown that in the absence of vitamin A, osteoblastic and osteoclastic activity in dogs is increased, and results in proliferation of cancellous at the expense of compact bony tissue; the main positions of the bony overgrowth are in the skull and vertebral column. One result is a rise in intracranial pressure and, after 4 to 8 months, compression of cranial nerves (E. Mellanby). Serious deficiency of vitamin A in animals causes hyperplasia of the gums with thickening and stratification of the

keratinous outer layers and of the sub-gingival epithelium; cells exfoliated from these form nests for bacteria. In moderate deficiency in man, the tongue and oral mucosa are pale and anaemic, smooth but unglazed; bleeding is uncommon and mobility or 'drifting' of teeth does not occur (J. A. Sinclair).

The opinion, that deficiency of vitamin A is an important cause of night blindness, has recently been shown to be clinically unsound.

Vitamin B₁

An analysis of the published work and a series of test cases with controls gives sound grounds for the conclusion that vitamin B₁ has neither a prophylactic nor a therapeutic effect on diphtheritic paralysis or on the cardiovascular complications of diphtheria. The patients gained only in appetite and in a sense of well-being (G. E. Donovan and M. Bannister). (See also pp. 5 and 50.)

Nicotinic acid

The frequency of glossitis, stomatitis, and Vincent's angina in pellagra which is cured by nicotinic acid has led to its trial in these conditions; in the cases so far reported, rapid improvement has occurred; the ulcers healed and the organisms disappeared from the mucosa (Sinclair). Glossitis of a type similar to that in pellagra occurs in sprue, pernicious anaemia, nutritional anaemias, and idiopathic steatorrhoea, and the successes in treatment suggest that nicotinic acid, and perhaps also riboflavin, are important for the treatment of these diseases which may have in common a deficiency of the B₂ complex (J. D. King; P. Manson-Bahr¹).

Vitamin C

Cases of moderate or sub-scorbutic deficiency of this vitamin, ascorbic acid, are becoming recognizable and it is worthy of comment that, when given with sodium bicarbonate, its storage by the adrenals and liver is increased and the excretion of the acid decreased (E. E. Hawley, J. P. Frazer, L. L. Button, and D. J. Stephens).

Acceleration in the healing process of wounds has been under discussion, and attention has been directed not only to the importance of an adequate protein diet, especially in severe burns, but also to the impairment in the formation of collagen fibres and to the failure of proliferating mesodermal cells to mature when there is a partial (sub-scorbutic) deficiency of vitamin C; this deficiency can also cause defective phagocytosis and haemorrhagic effusions, and may account for disruption of wounds after surgical operations. In human beings lack of vitamin C may retard healing, and when rapid healing is desirable, or after major operations, especially if a hollow viscus is opened, and after all serious wounds, 1,000 milligrams (15 grains) of ascorbic acid are recommended for three days to produce saturation and 100 milligrams (1½ grains) daily to maintain it; if oral dosage is impossible, the intramuscular or intravenous route should be employed (Annotation (1941) *Brit. med. J.*, 1, 560 and 568; A. H. Hunt).

Deficiency of vitamin C alters the intercellular substance of the periodontal tissues which become soft, less fibrous, and prone to bleed; the gums and tongue become red and swollen, and the teeth loose and 'drift' with resultant mal-occlusions (Sinclair; R. W. Keeton; H. J. Leonard; F. S. Roff and A. J. Glazebrook). Acute and chronic gingivitis and periodontoclasia are commonly associated with lack of vitamin C, and its administration in doses of 300 milligrams (5 grains) of ascorbic acid daily has, without dental treatment or mouth washes, been shown to be curative in gingivitis (H. G. Campbell and R. P. Cook). Although ascorbic acid increases the numbers of erythrocytes and haemoglobin percentage in scurvy, it lowers the erythrocyte count in artificially induced polycythaemia and prevents cobalt polycythaemia in rabbits; there is evidence also that it regulates the haemoglobin level, because the haemoglobin percentage in scurvy varies with the dosage of vitamin C (A. G. Barron and E. S. G. Barron).

Two cases of polycythaemia treated with 300 to 400 milligrams (5-6 grains) ascorbic acid along with 1 oz. of sodium bicarbonate daily showed that, although vitamin C alone had little effect, the combination of vitamin C with bicarbonate, possibly by increasing retention, led to a fall in the erythrocyte count, a decided polyuria and an improvement in health (J. Deeny).

Vitamin E

In the form of wheat-germ oil and α -tocopherol (9-18 milligrams ($\frac{1}{4}$ - $\frac{3}{4}$ grain) daily),

vitamin E gave promise of improving muscular dystrophies, amyotrophic lateral sclerosis, progressive muscular atrophy, bulbar paralysis, and tabes dorsalis. Recent clinical reports have not substantiated earlier claims, and the urinary excretion of creatine—a useful criterion of improvement—is not reduced in man. Even in association with vitamin B, uniform successes have not been achieved and critical assessment of its clinical value is desirable.

Vitamin P

The precise constitution of the natural vitamin is still undetermined although hesperidin is commonly used as its equivalent. Deficiency of vitamin P does not produce scurvy nor does its administration (1 gramme (15 grains) per day) influence the large, spontaneous, subcutaneous, or gingival haemorrhages, tissue hydration, anaemia, or general symptoms of scurvy, as does adequate dosage with vitamin C; but vitamin P increases the capillary resistance in scorbutic patients which vitamin C cannot do. Deficiency of vitamin P can occur in man even when he is receiving large amounts of ascorbic acid; the clinical symptoms of deficiency are weakness, lassitude, easy fatigue, pains in the legs on exertion, pain across the shoulders, and the occurrence of spontaneous petechial haemorrhages in areas of skin subject to pressure; these symptoms are curable by vitamin P (H. Scarborough). Conclusions cannot yet be reached on the part played by vitamin P; ascorbic acid in doses of 100 milligrams ($1\frac{1}{2}$ grains) daily in children (1½ to 6 years) is stated to improve cases of capillary fragility within a week (N. U. Kahn and M. Minn).

Vitamin K

The importance of vitamin K in the prevention and treatment of haemorrhage in hepatic and biliary diseases associated with jaundice is established. Of the synthetic compounds with vitamin K activity, 2-methyl-1:4-naphthoquinone appears to be about three times more potent than the natural vitamin; it is a yellow crystalline substance, only slightly soluble in water and, hence, inconvenient for injection; it is claimed, but confirmation is desirable, that given in tablet form it can be absorbed, without the addition of bile salts, from the intestine and that 2 milligrams ($\frac{1}{8}$ grain) thrice daily raises the prothrombin content to normal in 24–48 hours.

For injection, 2-methyl-1:4-naphthohydroquinone-3-sodium sulphonate or 'hykinone', a water-soluble compound, is supplied in isotonic solution so that 1 cubic centimetre is equivalent to 2 milligrams of 2-methyl-1:4-naphthoquinone; intravenous injection (dose 1–3 cubic centimetres (15–45 minims) of the solution) is useful for checking active haemorrhage, which is controlled within $1\frac{1}{2}$ to 3 hours; and a normal prothrombin level is reached in 24 to 48 hours, but it falls rapidly; an intramuscular injection maintains the normal level for some days (R. Kark and A. W. Souter).

Another compound, 2-methyl-1:4-naphthohydroquinone disuccinate, is also water-soluble, although unstable, and must be dissolved just before intravenous injection; its action is much more rapid but less sustained (J. Reid).

It should be recollected that vitamin K will not influence haemorrhage unless this arises from a deficiency of prothrombin in the blood. It has been shown that the administration of vitamin K (2 milligrams ($\frac{1}{8}$ grain) daily) to mothers for a week before labour increases the prothrombin content in the blood of the new-born infant, which may also receive 2 milligrams soon after birth as a prophylactic against haemorrhagic disease of the new-born (Kark and Souter). (See also pp. 5 and 50.)

PHENOTHIAZINE (THIODIPHENYLAMINE; 'PHENOVIS')

This lemon-yellow powder, insoluble in water and tasteless, is a thiazine dye with anthelmintic powers. It is available in tablets of 0.5 gramme (8 grains) and 1 gramme (15 grains) made with ox bile and as a granular preparation flavoured with lime juice for children. Small repeated doses are stated to be more toxic than occasional large ones. It is most effective against roundworms and threadworms.

In a mixed infection, 8 grammes (120 grains) of phenothiazine in powder on three successive mornings followed by 12 grammes of sodium sulphate in solution expelled dead roundworms and eliminated their ova from the faeces; some dead threadworms were expelled, but hookworm and whipworm eggs were undiminished.

In the treatment of oxyuris vermicularis, the dosage for children is: for under 4 years 1 gramme (15 grains), under 8 years 2 grammes (30 grains), and for adults 8 grammes (120 grains) daily for 7 to 10 days. Clinical cure is achieved without the use of enemas, anal itching soon ceases thus lessening the risk of reinfection, and the result is per-

manent. Expelled worms are often tinged red; the dye is excreted in the urine, which becomes pink within 20 minutes of administration and remains so for 2 days after treatment ceases; it also acts as a urinary antiseptic (Manson-Bahr²).

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PART III

ABSTRACTS OF MEDICAL LITERATURE

ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES

See also B.E.M.P., Vol. I, p. 1; Cumulative Supplement, Key Nos. 1-11; and Surveys and Abstracts 1939, p. 181; 1940, p. 141.

Conditions Simulating Acute Appendicitis

'Spinal appendicitis'

Under this title C. B. Rich describes cases of pain referred to the right iliac fossa from disease of the dorsi-lumbar region. This referred pain is comparable to sciatica from pressure on nerve structures due to displacement of the nucleus pulposus into the spinal canal, strain of the intervertebral ligaments, and from inflammation and swelling around the apophyseal joints in the lumbo-sacral region. Similar causes in the dorsi-lumbar portion of the spinal column may imitate appendicitis, but this sequence of events has been much neglected. This area of the spine, at the junction of a fixed and a mobile portion, is subject to unusual strain and repeated slight injuries, connected with faulty posture, especially in the period of growth. By diminishing the resistance of the spinal tissues these mechanical factors favour inflammation, which spreads into the spongy bone of the vertebral bodies causing condensation and which may narrow the spinal canal. Rich collected 50 cases of 'spinal appendicitis' in 1938-40, and states that the prolapse of the nucleus pulposus may be unilateral, cause scoliosis, and therefore strain on the apophyseal joint on one side only. Another factor explaining this prominence of right-sided pain is psychological, namely, fear of appendicitis, the pain on the left side being often neglected and only brought out by questioning. Most of these patients have lost a friend from appendicitis and operation. Appendicectomy sometimes removes the fear of appendicitis, though the pain may persist. Though there is not any direct radiological evidence there is circumstantial evidence, such as narrowing of the intervertebral disk at this region, early spondylitis with lipping, and other less common but better recognized causes of referred pain, such as tuberculosis, compression-fracture, and osteitis deformans. The condition may be acute or chronic. The pain is relieved by rest on the back, and aggravated by movement, active or passive; the temperature and leucocyte count are normal, nausea and vomiting are absent, and scoliosis, poor posture, and exaggeration of the normal curves may be present. In treatment it is important to correct the mechanical factors and to remove the phobia of appendicitis.

Acute Intestinal Obstruction

Acute intestinal obstruction due to gall-stones or endoliths

Recurrent gall-stone ileus.—P. R. Hinchey reports a case of recurrent gall-stone ileus in a woman, aged 79, who had 2 attacks of acute intestinal obstruction within 3 months; each attack required jejunotomy, and was followed by recovery. The calculi causing the obstruction measured $3.0 \times 3.0 \times 3.0$ centimetres and $3.2 \times 3.2 \times 2.9$ centimetres, and weighed 12.7 grammes and 19 grammes respectively. Before the first attack the patient had passed in the stools a stone measuring $3.2 \times 3.0 \times 2.0$ centimetres and weighing 13.2 grammes.

Torsion

Torsion of great omentum

Affecting an appendix epiploica.—In a report of a case of chronic torsion of an appendix epiploica A. D. Le Vay points out that out of 60 recorded cases of torsion and inflammation of these appendices, 46 were acute, 9 chronic, and 5 symptom-free. All but 6 were cases of torsion, and these 6 occurred in hernial sacs. Acute cases are rarely diagnosed before operation. The isolated symptom of pain in the left iliac fossa in a patient of middle age should suggest the possibility of chronic disease of an appendix epiploica on the sigmoid flexure.

Mesenteric Thrombosis and Embolism

Symptoms

T. Moore reports 8 cases of mesenteric vascular occlusion. The cause is either (a) arterial obstruction due to embolism or thrombosis, or (b) venous obstruction due to thrombosis. The disease is characterized by the sudden onset of central abdominal pain. Constant abdominal pain persists, but is associated with severe attacks of colic. Vomiting is generally severe, everything taken by mouth being immediately returned. The abdomen becomes progressively distended. The patient is pale and restless, the blood pressure is low, and the pulse poor and rapid. After an enema the evacuation of blood-stained fluid is almost diagnostic. Abdominal exploration should be carried out as soon as possible, and the infarcted portion of intestine removed.

Chronic Intussusception*Clinical picture*

N. F. Kirkman reports a case of chronic intussusception in a woman, aged 44, apparently dating from an acute intussusception in early childhood. There had been periodical attacks of abdominal colic, and in 1933 appendicectomy was performed, but without any benefit. In 1939 laparotomy and a lateral anastomosis of the ileum with the pelvic colon was performed, but without any relief. Later hemi-colectomy was carried out, and the patient made a successful recovery. In an anatomical note on the specimen T. Barlow and S. Mottershead conclude that the condition was probably derived from a simple ileocolic intussusception and that part of the entering and returning layers of the intussusception had sloughed away on the anti-mesenteric border from the region of the ileocaecal valve to about 3 inches from the apex of the intussusception.

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ABORTION

See also B.E.M.P., Vol. I, p. 47; Cumulative Supplement, Key No. 12; Surveys and Abstracts 1939, pp. 30 and 182; 1940, p. 141; and p. 17 of this volume.

Clinical Aspects of Abortion*Threatened and habitual abortion*

Pregneninolone therapy.—L. Krohn and J. M. Harris employed pregnenolone (anhydro-hydroxy-progesterone) orally in 50 cases of threatened and habitual abortion. In this series there were only 8 failures. The results obtained compared favourably with those from the use of progesterone in oil. No undesirable or toxic effects were noted. The dosage of the drug was 10 milligrams twice weekly until quickening occurred.

Incomplete abortion

Value of conservative treatment.—H. P. Mencken and H. H. Lansman report good results from the conservative treatment of abortions in which the infection is apparently limited to the uterus. Among 600 incomplete abortions studied the only fatality followed radical therapy. Patients with an extra-uterine infection should be treated conservatively. Sulphanilamide is the most recent drug to be used. In *Streptococcus haemolyticus* infections the drug reduces the morbidity and has saved some of the hitherto hopeless cases. Even the slightest manipulation may spread infection. Digital vaginal examination has often caused exacerbations in infected abortions; it should be reserved only for cases of doubtful diagnosis, or for those in which immediate surgical intervention for localized pus is contemplated. Otherwise the patient should be examined only after a five-day afebrile period.

Artificial and Intentional Abortion*Tetanus as a sequel*

W. L. Bush reports on 5 cases of a rare accident, namely, tetanus following induced abortion. All 5 patients consulted the same medical practitioner within 2 weeks, and had gauze packs placed in the cervix 6 or 7 days before admission to hospital. The usual symptoms were stiffness of the neck and jaws and reflex muscular spasms. In no case was there evidence of previous wounds or punctures. Treatment varied in each case, but always included doses of tetanus antitoxin varying from 66,000 units to 180,000 units. Avertin with amylene hydrate was given in most cases. The patients all died within 3–5 days. It is concluded that all the patients were infected with the same virulent strain of tetanus bacilli.

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Krohn, L., and Harris, J. M. (1941) *Amer. J. Obstet. Gynec.*, **41**, 95.

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ABORTUS FEVER

See also B.E.M.P., Vol. I, p. 68; Cumulative Supplement, Key No. 13; and Surveys and Abstracts 1939, p. 183; 1940, p. 143.

Bacteriology*Morphology*

Reaction to sulphonamides.—According to E. W. Goodpasture *Brucella abortus*, like *Bacterium tularensis*, is entirely dependent upon an intracellular position for growth in the living unaltered tissues. The invaded host cells seem to act as a stimulus or to supplement a deficiency in these parasites of which advantage is readily taken. In the one event the cellular parasitism is for the invader only an adventitious relationship, in the other it is an advantage. As *Brucella abortus* is an essentially intracellular parasite, it is unlikely to react to sulphonamide drugs.

Incidence in Man*Laboratory infection*

H. N. Green reports 3 cases of laboratory infection with a stock strain of *Brucella abortus*,

which had been continuously subcultured for 2 to 3 years and in 2 instances was known to be resistant to sulphanilamide. In none of the 3 laboratory assistants was the site established, or method of entrance of the infection, such as a skin abrasion, droplet infection, or from transmission to the mouth by contaminated fingers. Although admittedly without any concrete evidence, it is tentatively suggested that the infection was due to inhalation of contaminated air in the vicinity of large concentrations of *Brucella abortus* growing on solid media; conceivably, when the cultures had become rather dry, air currents, induced by Bunsen burners, might dislodge micro-organisms from surface cultures.

Goodpasture, E. W. (1940) *Trans. Studies Coll. Phys. Phila.*, 4 ser., 9, 11.

Green, H. N. (1941) *Brit. med. J.*, 1, 478.

ACCESSORY SINUSES OF THE NOSE

See also B.E.M.P., Vol. I, p. 77; and Surveys and Abstracts 1939, p. 183; 1940, p. 144.

The Accessory Sinuses of the Nose

Inflammatory diseases

Lipiodol radiography of antrum.—J. M. Robins claims that lipiodol radiography is an important method of investigating the maxillary sinuses and that it should be done in all cases in which there is any doubt about the nature of the mucosa lining the maxillary antrum, which can seldom be determined with any degree of accuracy by plain radiography. Polypi and chronic maxillary sinusitis can be diagnosed with much greater accuracy by this method. There are two methods of introducing lipiodol into the antrum; one is injection by an antrum trocar and cannula through the inferior meatus of the nose, and the other is the replacement method. The author recommends the former.

Sinusitis

Relation to bronchiectasis.—R. L. Goodale states that sinusitis often accompanies bronchiectasis. It may be present at the onset of the chest infection, or may appear later. In patients with sinusitis there may be a considerable amount of sputum from the upper respiratory tract even after operation on the chest. Patients unsuitable for lobectomy have been improved locally, after surgical treatment of sinus infections, and, in some mild cases of bronchiectasis, the chest symptoms have also improved.

Acute sinusitis

X-ray therapy.—H. L. Williams and W. C. Popp employed X-rays in cases of acute sinusitis with satisfactory results. In patients with symptoms of 1 to 5 days' duration, doses of 50 roentgens were used; in cases with symptoms of longer duration doses of 75 to 100 roentgens were employed. From 1 to 3 treatments, according to response, were given on alternate days. The voltage was 130 kilovolts, filtration 6 millimetres of aluminium for adults and 4 millimetres for children. The distance was 40 centimetres. If more than one sinus was involved, all those affected were treated. The most striking effect of treatment was the relief of pain and headache. There was a notable increase in the discharge. Better results were obtained when the treatment was begun early, and the results appeared to be better in an initial attack than in recurrences after one or more attacks.

Infection after acute frontal sinusitis.—P. C. Bucy and W. T. Haverfield, on the basis of 4 cases of cranial, intracranial, and combined infection after acute frontal sinusitis, and from a review of the literature, come to the following conclusions: the infection generally spreads to the frontal bone and invades the brain by way of the venous system. Prevention of the fulminating frontal sinusitis, osteomyelitis, and cerebral abscess which so often result from swimming, can in some measure be attained by instruction regarding proper breathing and the use of protective devices. The chief preventive measures, however, must be directed towards prevention of the spread of infection; this can best be obtained by prompt external surgical drainage in the acute fulminating cases. Osteomyelitis of the skull should be treated by excision of all the infected bone as soon as the diagnosis is made. Cerebral abscess should be drained through an uninfected area of the skull, if possible, with due attention to prevention of infection of the meninges.

Chronic sinusitis

Treatment by X-rays.—N. A. Youngs reports on the result of radiological treatment of 75 cases of chronic sinusitis. He obtained cures in 16 cases, great improvement in 31, but no improvement in 28. After this treatment many of the patients reported less susceptibility to the common cold. In 2 cases polypi of moderate size disappeared for several months after treatment.

Chronic suppuration

Treatment by sodium salt of sulphathiazole.—F. M. Turnbull reports on the use of a nasal spray of 5 per cent solution of the sodium salt of sulphathiazole in chronic sinusitis. He obtained greater relief from symptoms than with any other preparation. In only 2 out of 47 cases were unfavourable symptoms noted, and these 2 patients presented swelling and blocking of the nose from hay fever. Of the 47 patients, 40 reported definite symptomatic relief, stating that the spray relieved congestion, opened the nasal passages, promoted drainage, and relieved pressure headaches. Granulocytopenia and haemoglobinuria were not observed.

Bucy, P. C., and Haverfield, W. T. (1940) *J. Amer. med. Ass.*, 115, 983.

- Goodale, R. L. (1940) *New Engl. J. Med.*, **223**, 654.
 Robins, J. M. (1941) *J. Laryng.*, **56**, 101.
 Turnbull, F. M. (1941) *J. Amer. med. Ass.*, **116**, 1899.
 Williams, H. L., and Popp, W. C. (1940) *Ann. Otol., etc., St. Louis*, **49**, 749.
 Youngs, N. A. (1941) *Arch. Otolaryng., Chicago*, **33**, 550.

ACHALASIA

See also B.E.M.P., Vol. I, p. 116; Cumulative Supplement, Key No. 18; and Surveys and Abstracts 1939, pp. 43 and 185; 1940, p. 145.

In the Alimentary Tract

Of the pharyngo-oesophageal sphincter (Plummer-Vinson syndrome)

Radiology.—A. S. Johnstone contributes some radiological observations on post-cricoid obstruction and anaemia, the syndrome described by A. Brown Kelly and by D. R. Paterson in 1919, but often called the Plummer-Vinson syndrome. Four cases of this nature examined radiologically all showed definite obstruction in the post-cricoid region, and the diagnosis of a web was made; endoscopy confirmed this in 3 cases, in the other case there was carcinomatous change in the adjacent mucosa. There is some difference of opinion about an organic fibrous web or one due to spasm, such as of the crico-pharyngeus muscle; but a fibrous web may form at the site of the spasm. Further, dry sticky mucus and leucoplakia may also cause dysphagia. Attention is drawn to the danger of an incomplete examination because malignant changes may occur in the lower part of the oesophagus or in the stomach. A form of dysphagia due to deficiency of iron and called sideropenic dysphagia has been described, and to some extent controlled by iron treatment (Waldenstrom and Kjellberg).

Of the cardiac sphincter

Supervention of squamous-celled carcinoma.—R. C. Brock records 2 recent cases, in men aged 43 and 51 years, with a history of cardiac achalasia in whom squamous-celled carcinoma supervened and proved fatal. In addition, the author retrospectively recognized 2 similar cases recorded by C. Hilton Fagge in 1872, or 43 years before A. F. Hurst, with the assistance of Cooper Perry, introduced the name and hypothesis of achalasia for the condition regarded as cardiospasm. Among 13 necropsies on achalasia of the cardia, G. W. Rake (1931) found 2 with squamous-celled carcinoma.

- Brock, R. C. (1940-41) *Guy's Hosp. Rep.*, **90**, 23.
 Fagge, C. H. (1872) *Guy's Hosp. Rep.*, ser. 3, **17**, 413.
 Hurst, A. F. (1915) *Quart. J. Med.*, **7**, 300.
 Johnstone, A. S. (1941) *Brit. J. Radiol. N.S.*, **14**, 177.
 Kelly, A. B. (1919) *J. Laryng.*, **34**, 289.
 Paterson, D. R. (1919) *J. Laryng.*, **34**, 285.
 Rake, G. W. (1931) *Lancet*, **2**, 682.
 Vinson, P. P. (1922) *Minn. Med.*, **5**, 107.
 Waldenstrom and Kjellberg (1937) *Acta. radiol., Stockh.*, **20**, 618.

ACIDOSIS

See also B.E.M.P., Vol. I, p. 145.

Physiology

Dehydration

Blood changes.—A. G. V. Aldridge reports the blood changes in 51 infants with varying degrees of dehydration; of these there were 35 with gastro-enteritis and 16 with pyloric stenosis. The red cell count was raised, the average being over 5,000,000 per cubic millimetre. The haemoglobin was also increased, though to a less degree than the red cell count, due to hypochromic anaemia. In gastro-enteritis the plasma chlorides varied, but on the average it was raised (651 milligrams per cent); it did not necessarily vary with the degree of dehydration or with the clinical condition. The apparent, if not actual, rise in chlorides was shown to be due to the relatively small amount of chlorides as compared with base, especially sodium, lost from the bowel; the concentration of the circulating blood; and renal insufficiency. In pyloric stenosis the plasma chlorides were either diminished slightly or on the low side of normal. Plasma protein in gastro-enteritis was slightly higher than in a series of normal infants. The plasma protein concentration cannot be taken as an indication of the state of hydration of the circulating blood.

Aldridge, A. G. V. (1941) *Arch. Dis. Childh.*, **16**, 81.

ACNE

See also B.E.M.P., Vol. I, p. 156; Cumulative Supplement, Key No. 23; and Surveys and Abstracts 1939, p. 185; 1940, p. 147.

Acne Vulgaris

Clinical picture

Psychological reactions.—W. Marshall, discussing the psychology of the general public with regard to acne vulgaris, mentions that improvement of the skin lesions often changes the patients' mentality from one of isolation and an asocial attitude to sociability. The withdrawal from society of the sufferers from acne is a self-induced reaction, and is correlated with the

withdrawal of the over-sensitized allergic patient from his immediate environment. It is motivated by a desire for self-preservation, especially of personality.

Cryotherapy

W. L. Dobes and H. Keil state that cryotherapy is an important adjuvant measure in the treatment of some types of acne, particularly the papulo-pustular and the hard indurated form. The technique consists of the application of a mixture of solid carbon dioxide, which has been ground to a fine powder in a mortar, and about 10 per cent of precipitated sulphur and enough acetone to form a thin paste. This mixture is applied on a tampon of absorbent cotton, covered by a square of gauze. Applications are made once or, in some cases, twice weekly. Each area or lesion is treated with enough pressure for about half a second to produce blanching of the spots. The sulphur precipitates on the skin as a yellowish residue which is allowed to remain for from 15 to 30 minutes. The authors state that the method is contraindicated in patients with smooth elevated pigmented naevi, in acne in the negro, immediately after X-ray therapy, and in sunburnt people. It is indicated in patients who have not responded to adequate amounts of X-ray or other local therapy, in patients below the ages of 17 or 18, in patients with dry skins, in those with resistant acne indurata, and in patients who refuse X-ray therapy. The authors have treated 115 cases. Recurrences were noted in 25 per cent of these.

Dobes, W. L., and Keil, H. (1940) *Arch. Derm. Syph., N.Y.*, **42**, 547.

Marshall, W. (1941) *Canad. med. Ass. J.*, **44**, 599.

ACROMEGALY

See also B.E.M.P., Vol. I, p. 166; Cumulative Supplement, Key No. 24; and Surveys and Abstracts 1940, p. 148.

Clinical Picture

Pain in the hands and feet

H. W. Woltman states that, in a review of 213 cases of acromegaly, 10 patients complained of a periodic pain in the hands, and 8 of a similar disturbance in the feet. It has been thought that the pain and paraesthesia were the result of interstitial neuritis, but the author suggests that the condition may have a vascular or metabolic basis, or may be related to proliferation of the perineurium and endoneurium.

Woltman, H. W. (1941) *Arch. Neurol. Psychiat., Chicago*, **45**, 680.

ACTINOMYCOSIS

See also B.E.M.P., Vol. I, p. 173; Cumulative Supplement, Key No. 26; and Surveys and Abstracts 1939, p. 186; 1940, p. 149.

Treatment

Sulphonamide compounds

L. Dobson, E. Holman, and W. Cutting report 3 cases of actinomycosis, one of the jaw, one of the lungs and ribs, and one of the abdomen, apparently cured completely by the use of sulphanilamide in association with iodides and X-rays. The authors conclude that sulphonamide compounds have a definite place in the treatment of this disease.

Abdominal actinomycosis.—G. C. Dorling and N. L. Eckhoff treated 5 cases of abdominal actinomycosis with sulphonamide compounds. Although all were severe infections, 4 patients recovered completely. In one case in which deep X-rays had also been employed, a later operation showed that all evidence of the disease had disappeared. The authors conclude that sulphonamide therapy should be tried early in all suspected cases of abdominal actinomycosis. In these cases sulphanilamide, sulphapyridine, or both, were employed; both appear to be effective. Two or three courses, each lasting a week, and with a week's interval, are generally necessary.

W. H. Ogilvie reports a case of abdominal actinomycosis with diffuse infection in which recovery followed sulphapyridine therapy. A girl, aged 22, with multiple sinuses in the abdominal wall, who had received large doses of potassium iodide and who had had surgical treatment without improvement, was given sulphapyridine in doses of 2 tablets, every 4 hours at first, reduced after 24 hours to 2 tablets every 6 hours. After 13 days of this treatment there was such a dramatic improvement in her local and general condition that the drug was discontinued. The discharge decreased rapidly from the first day of treatment, and the wounds had healed up 13 days after cessation of treatment. Laparotomy, performed 2 months later for repair of a ventral hernia, did not show any evidence of actinomycosis.

Dobson, L., Holman, E., and Cutting, W. (1941) *J. Amer. med. Ass.*, **116**, 272.

Dorling, G. C., and Eckhoff, N. L. (1940) *Lancet*, **2**, 707.

Ogilvie, W. H. (1940) *Brit. med. J.*, **2**, 254.

ACTINOTHERAPY

See also B.E.M.P., Vol. I, p. 180; Cumulative Supplement, Key No. 27; and Surveys and Abstracts 1939, p. 187; 1940, p. 150.

Artificial Light Treatment

Carcinogenic effect of ultra-violet rays

H. P. Rusch, B. E. Kline, and C. A. Baumann, investigating the carcinogenic effect of ultra-

violet light, found that the carcinogenic wave-lengths of the spectrum were between 2,900 and 3,341 Ångström units. Wave-lengths of 2,537 or 3,341 Ångström units and above were not carcinogenic. The carcinogenic wave-lengths thus coincided partly with those most potent in the production of erythema. Radiant energy, however, with a wave-length of 2,537 Ångström units, produced erythema without the formation of tumours.

Post-irradiation necrosis

A. Eidinow discusses the irradiation treatment of post-irradiation necrosis, and states that, for acute erythematous dermatitis, massive ultra-violet irradiation, equivalent to 10 times the normal erythema dose, should be applied to the lesion and to the area of normal skin extending half an inch beyond the lesion. Treatment should be given at intervals of 14 days until healing is established. Daily exposure to the infra-red rays of a 1,000-watt tungsten-filament lamp for 20 to 30 minutes alleviates painful symptoms. Telangiectases, after the application of the diathermy current, should have similar treatment. Post-irradiation warts may sometimes be dispersed by massive ultra-violet irradiation. Subacute and chronic ulceration may likewise be benefited by a combination of ultra-violet and infra-red therapy.

Technique

General irradiation

Irradiation of air in hospitals.—F. del Mundo and C. F. McKhann state that ultra-violet irradiation of the air in children's hospitals appears to reduce the incidence of infections. In a control ward the incidence of infections during the winter of 1939-40 was 12.5 per cent, whereas in a similar ward, the cubicles of which were protected across the fronts and tops by ultra-violet irradiation, the cross-infection rate was 2.7 per cent.

Eidinow, A. (1941) *Brit. J. Derm.*, **53**, 171.

del Mundo, F., and McKhann, C. F. (1941) *Amer. J. Dis. Child.*, **61**, 213.

Rusch, H. P., Kline, B. E., and Baumann, C. A. (1941) *Arch. Path.*, **31**, 135.

ADENOIDS

See also B.E.M.P., Vol. I, p. 193; and Surveys and Abstracts 1939, p. 187; 1940, p. 151.

Treatment

Operative technique

V. E. Negus describes the clearance mechanism of the nose and pharynx in relation to the removal of adenoids. Debris and bacteria are passed down by nasal ciliary action and deposited in the nasopharynx. Swallowing muscles pass it down to the stomach. Accumulations of debris harbour infection. This double process may be interrupted by adenoid growths which collect debris in their crevices; by injury of the ciliated epithelium which may regenerate but without the same coordination and direction as before; by the injury to the muscular mechanism of swallowing and by scarring of the fauces and tonsillar fossae which may interfere with the closure of the nasopharynx. Removal of the adenoids must be complete and accurate. Persistent remnants, which may become fibrous, harbour infection which may be transmitted to the trachea and bronchi. A transverse ridge often found after operation behind the velum with a depression above it is caused by downward displacement of aponeurosis and muscle fibres. Damage to the Eustachian cushions may be avoided by insertion of the gloved finger behind the soft palate, between them and the adenoid mass, and by squeezing the latter towards the centre of the nasopharynx. For removal the author recommends the use of a correct pattern of an adenotome of La Force type. Lateral guides ensure that only the adenoids are removed. The nasopharyngeal wall should feel smooth after the operation. Any lymphoid tissue in the fissure of Rosenmüller has probably been pushed there by splaying of the curette and there should be none if preliminary centring is carried out. Haemorrhage may be stopped by insertion of a sponge soaked in protargol behind the palate for 5 minutes. Until the regeneration of the ciliated epithelium is completed there is immediate danger of otitis media. The author suggests that sinusitis in children may be due to the presence of adenoids.

Negus, V. E. (1941) *J. Laryng.*, **56**, 119.

ADIPOSIITY

See also B.E.M.P., Vol. I, p. 202; and Surveys and Abstracts 1939, p. 188; 1940, p. 152.

Treatment

Obese children

Benzedrine sulphate.—R. H. Kunstadter reports on the administration of benzedrine sulphate to 30 obese children between the ages of 2½ and 16 years. The children were selected after they failed to lose weight on a prescribed reducing diet, and, in some cases, in addition after thyroid extract. The average weekly loss of weight among 26 children who received continuous treatment for more than 2 weeks was 0.831 pound per week. The greatest loss of weight occurred during the first 2 weeks of treatment. The effect of the drug on the pulse rate and blood pressure varied. Of the 30 patients, 40 per cent had unpleasant reactions at the beginning of treatment. Loss of weight was primarily due to loss of appetite with consequent decrease of food intake.

Harmful effect of endocrine therapy.—H. Bruch reports (a) the case of a boy, aged 6 years, in whom marked obesity developed while he was receiving gonadotrophic substance, and

(b) the case of an 11-year-old girl who became obese after a thyroid enlargement had been noted. In both cases the obesity was shown to be in causal relation to the diagnosis and treatment. The latter stimulated an over-anxious attitude of the families which led to over-feeding and restriction of activity, and thus to obesity. The author considers that the diagnosis of an endocrine disorder in an obese child, and long-continued endocrine treatment, are both unjustifiable and harmful, since they produce or increase the apprehensive attitude of the parents.

Bruch, H. (1941) *J. Pediat.*, **18**, 36.

Kunstadter, R. H. (1940) *J. Pediat.*, **17**, 490.

ADRENAL GLAND DISEASES

See also B.E.M.P., Vol. I, p. 232; Cumulative Supplement, Key No. 30; and Surveys and Abstracts 1939, pp. 109, 166 and 189; 1940, p. 152.

Adrenal Hypoplasia and Insufficiency

Addison's disease

Clinical picture.—In a review of the recognition and treatment of Addison's disease R. A. Cleghorn draws attention to a defective distribution of secondary hair, more often due to atrophy of the adrenal cortex than to destruction of the adrenals by tuberculosis; this may be of help in arriving at a decision about the nature of the responsible morbid lesion. It is suggested that hypothyroidism is associated with Addison's disease more often than is realized. In 4 cases this was clinically obvious in 2, and in the other 2 the exceptionally low basal metabolic rate suggested the therapeutic trial of thyroid extract; this proved to be effective. But it is definitely pointed out that in the depressed metabolism present in Addison's disease, without an underlying hypothyroidism, the administration of thyroid preparations is ineffective and dangerous. Desoxycorticosterone acetate was given to 12 patients by hypodermic injection for 16 to 3½ months, after they had been previously treated by cortin and salt. Of the 12 patients one died and another has entered a remission and does not need hormonal treatment, an exceptional case. The remaining 10 patients were then treated by subcutaneous implantation of crystalline desoxycorticosterone acetate pellets; in 4 the results were good and in 2 fair. In the other 4 the results were poor; after a few weeks of apparently satisfactory progress 3 of the patients suffered from loss of appetite, hypoglycaemic attacks, oedema of the ankles, cardiac irregularity, and falling blood pressure, due to cardiac failure. The fourth patient received one pellet only without added salt, but became oedematous from the outset. Two patients improved when aqueous cortical extract was given as well as desoxycorticosterone acetate. On this evidence and on experimental grounds it seems probable that desoxycorticosterone is not a complete substitute for adrenal cortex.

Value of the potassium tolerance curve in diagnosis.—J. A. Greene, H. Levine, and G. W. Johnston discuss the question whether or not the potassium tolerance curve is of value in the diagnosis of adrenal cortical deficiency in man. They record a normal curve in 2 cases of Addison's disease, and an abnormal in some other conditions, including bromide intoxication. They conclude that the test is not specific for adrenal cortical insufficiency in man.

Sublingual administration of desoxycorticosterone acetate.—D. Turnoff and L. G. Rowntree report the successful treatment of 2 advanced cases of Addison's disease by the sublingual administration of desoxycorticosterone acetate in propylene glycol. The patients were given 1 milligram (6 drops of solution) under the tongue, 6 to 7 times daily. The preparation was retained for 15 minutes, and then expectorated. Sodium chloride was given early in the treatment, but, because of the oedema which it produced, its use was discontinued.

Implantation of desoxycorticosterone acetate pellets.—R. C. Mochlig has successfully treated a patient with Addison's disease by implantation of the synthetic cortical hormone, desoxycorticosterone acetate. The patient was a man aged 31, first seen in January 1937 with the distinguishing features of Addison's disease. His weight was 117 pounds and the blood pressure fluctuated between 68/44 and 72/56 millimetres of mercury. The patient was given 5 cubic centimetres daily of adrenal cortical extract parenterally and 10 grammes of sodium chloride orally. After 1 week he was discharged from hospital greatly improved and with blood pressure 98/62. Subsequently he received on 6 days a week 2 cubic centimetres of adrenal cortex extract and 2 cubic centimetres of pituitary growth extract, given in the hope of stimulating the cortical tissue. One month after he was first seen his weight was 133½ pounds and his blood pressure 102/64, and in a further week he returned to work. He was then instructed to take 2 cubic centimetres of adrenal cortical extract daily and to continue the sodium chloride. In August the sodium chloride was discontinued and the patient on his own initiative discontinued the cortical extract. Twelve days after this cessation he was in a typical Addisonian crisis, but after receiving 10 cubic centimetres of adrenal cortical extract and sodium chloride he improved and the dosage was reduced to 2 cubic centimetres of cortical extract daily. His career was uneventful until June 1939 when he discontinued treatment for 2 weeks and his blood pressure fell to 88/60. Five cubic centimetres of cortical extract and 10 grammes of sodium chloride were administered.

On June 30th, 1939, 5 milligrams of desoxycorticosterone acetate in sesame oil were given, and the dose was repeated daily, except on Sunday; the salt was discontinued one week later. On July 18th his blood pressure was 114/74 and his weight 136 pounds. On September 7th,

1939, 4 pellets each weighing 150 milligrams of desoxycorticosterone acetate were inserted subcutaneously over the middle portion of the left abdomen. By September 23rd the blood pressure had risen to 122/86 and the patient felt well. At the time of publication, 10 months after implantation of the tablets, the patient was reported to be still doing very well without further medication, though there had been no change in the pigmentation of the skin.

Cardiac failure after desoxycorticosterone.—D. M. Willson, E. H. Rynearson, and T. J. Dry record the case of a woman, aged 33 years, with Addison's disease; after daily subcutaneous administration of 5 milligrams of desoxycorticosterone acetate in oil, later increased to 7.5 milligrams, she gained weight, the blood pressure fluctuated, at a level much above that usual in the disease, and slight oedema of the ankles appeared; the dose was then reduced to 5 milligrams. Later it was recognized that she was suffering from acute myocardial embarrassment and not from a crisis of adrenal insufficiency, but the dose of 3 milligrams of desoxycorticosterone acetate was given daily and increase in potassium salts and a diminution in sodium salts prescribed; improvement followed. The diagnosis between an Addisonian crisis and the toxic symptoms due to the synthetic desoxycorticosterone effects depends on hypertension and oedema; a simple physical sign is described: all that is needed is to observe the point at which the peripheral veins collapse when the patient's hand is slowly raised above the level of the heart: in the crises of Addison's disease the veins are collapsed; in congestive heart failure venous congestion is the rule, and its presence excludes the possibility of crisis in adrenal insufficiency.

Adrenal grafting.—F. Katz and F. Mainzer report a very successful operation in a woman, aged 56 years, of grafting an adrenal from a man aged 52 years just recently dead of a cerebral tumour and of the same blood group. She had been given anterior pituitary extract for several weeks without any result; but she responded well to cortical extracts and for a year all went well; then a severe relapse occurred, and the left adrenal from the man, mentioned above, was grafted into her abdominal wall under local anaesthesia. Soon after the operation the symptoms of adrenal insufficiency reached their climax—increased somnolence, uncontrollable vomiting, frequent diarrhoea, collapse of circulation, and fall of blood pressure to 60 millimetres of mercury, in spite of increase of the daily administration of cortical extract to 80 grammes and that of salt to 50 grammes. But within 3 days of the operation the condition improved, the amount of the cortical extract was reduced, and after the seventh day discontinued, and she felt perfectly well. She left the hospital on the sixth day, and during the next 2 months the systolic blood pressure varied between 115 and 135 millimetres of mercury; but any considerable exertion or excitement always caused slight somnolence, and pain in the back, and during an attack of influenza the blood pressure fell to 80 millimetres of mercury, when it was necessary to give 10 to 20 cubic centimetres of cortical extract daily. Fifteen months after the operation the results continued to be excellent. Stress is laid on the importance of the donor and recipient in grafting operations belonging to the same blood group. The publication of this case was followed by criticism of the accuracy of the diagnosis; J. J. Conybeare suggested that possibly a better title for the paper would have been 'Grafting of adrenal gland in a case of suspected Addison's disease'.

Incomplete syndromes

Acute bilateral adrenal haemorrhage.—J. W. Lindsay, E. C. Rice, M. A. Selinger, and L. Robins report 7 cases of acute bilateral adrenal haemorrhage with purpura, ranging from 6 months to 6 years, and bringing up the total number of recorded cases to 96. It has been stated that 70 per cent of the cases occur in children under 2 years of age. Within 8 to 12 hours a striking cyanosis occurs, and may be followed by purpura. The temperature may be high or below normal, the pulse and respirations are rapid. In their review of the subject the authors, all working pathologists, conclude that the meningococcus is responsible for the majority of cases and that most of the remaining cases are due to *Haemophilus influenzae*. P. B. Blaher and B. E. G. Bailey (1901) suggested that the cause was haemorrhagic smallpox. The authors use the eponymous title Waterhouse-Friderichsen syndrome; R. Waterhouse collected 16 cases in 1911, and Friderichsen reviewed the subject in 1918. It may, however, be pointed out that in 1898 G. F. Still collected 18 cases, and that at the same meeting of the old Pathological Society of London other cases were reported by F. W. Andrewes, A. E. Garrod, J. H. Drysdale, and F. E. Batten.

Adrenalectomy effects in rats.—W. O. Reinhardt and R. O. Holmes record the results of adrenalectomy in rats on the thymus, lymphatic glands, and spleen. It is first pointed out that the existence of a relation between the thymus and the adrenal cortex is well established; adrenalectomy has been reported as causing thymus regeneration and it has been shown that cortin and adreno-corticotrophic hormones cause thymic involution. Clinically there seems to be a relation between adreno-cortical hypofunction and enlargement of the thymus and lymphoid tissues. In the experimental research 60-day-old normal male rats of the Long-Evans strain were used: 60 rats were submitted to a one-stage bilateral adrenalectomy, life being prolonged by 1 per cent sodium chloride solution; 44 animals survived the 45-day experimental period without any macroscopically visible evidence of adrenal cortex at necropsy. As salt controls, 34 animals were maintained on 1 per cent sodium chloride solution; and 30 animals were given tap water. The thymus and lymphoid tissues are heavier in the adrenalectomized animals than in the controls. Sodium chloride *per se* appears to cause slight increase of weight in the thymus and the reverse effect in the lymphatic glands. The response

of the systemic lymphatic glands is similar to, and even more pronounced than, that of the thymus, but the mesenteric lymphatic glands are less affected. The spleen reacts in the same way as the thymus and lymphatic glands. Microscopic examination shows that the heavier weight of the lymphatic tissue is due to an increase in bulk of the normal elements and not to any specific morphological change. The results are of special interest in connexion with so-called lymphatism.

Hyperfunction of the Adrenal Cortex: Hyperplasia and Neoplasm

Clinical picture

Feminism.—L. R. Broster reports the case of a man of 32 with the condition of feminism. His bodily contour was distinctly feminine. His height was 5 feet 5 inches, his weight 8 stone 5 pounds, and his pelvic girdle (31 inches) wider than the pectoral (30 inches). The external genitalia were small, and the pubic hairs sparse. His sexuality was more or less neuter. His mentality was good, but his temperament was somewhat unstable. He was treated with endocrines and by testicular grafts without result. Laparotomy showed that both adrenals were larger than normal, and the left adrenal was removed. Histological examination showed that the cortical cells were normal, but that they gave the positive ponceau-fuchsin reaction, of moderate degree. After the operation the patient improved greatly, both physically and psychologically.

Renal hypernephroma and virilism.—J. Tenenbaum records the complicated and rare condition, in a woman aged 37, of a primary renal hypernephroma with virilism, which was associated with metastases and hyperplasia of the cortex of both adrenals. The clinical picture included a systolic blood pressure of 102/60 and a diastolic of 60 millimetres of mercury, intermittent haematuria, occasional renal colic, emaciation, masculine features, cheeks and chin covered with a beard-like growth, anaemia, a leucocyte count of 14,300 with 90 per cent polymorphonuclears, a fixed nodular mass in the right upper quadrant of a scaphoid abdomen, radiologically a large calculus in the left kidney, staphylococci and blood in the urine, and a temperature of 102° F. on admission. Necropsy showed a large primary hypernephroma (carcinoma) occupying the lower half of the right kidney with numerous small nodules in the upper part of that kidney. There were wide-spread metastases in the adrenals, the cortices, the left kidney, lungs, and tracheobronchial lymphatic glands. The left kidney contained three calculi and its pelvis much pus. The author leaves open the question whether or not the metastases and hyperplasia of the adrenal cortex should in this case be regarded as responsible for the unusual association of virilism with a renal hypernephroma.

Melano-carcinoma of the adrenal gland

With wide-spread metastases.—An unsigned study from the Institute of Pathology, Belfast, discusses the clinical, and especially the pathological, features of the case of a man, aged 59, who came under observation with paresis of the left arm and leg of slow onset, resembling the effect of cerebral thrombosis. He also had several pigmented subcutaneous spots on the front and back of the chest. The necropsy showed wide-spread melanomas in the liver, spleen, heart, lungs, skin, tongue, oesophagus, stomach, brain, thyroid, pituitary, kidneys, pancreas, and intestines. Both adrenals were much enlarged by growth. The right precentral gyrus was partly occupied by a melanoma, 1.5 centimetres in its greatest diameter, around which there was a recent cerebral haemorrhage. Histologically the tumour was regarded as a melano-carcinoma. The two commonest sites for a primary melanoma—the eye and the skin—were excluded, and the adrenal origin, though the bilateral involvement militates against this view, was suggested, the cortex, and not the medulla, being the starting point. The metastases were ascribed to blood and lymphatic transport. The pathological discussion raises other points of interest: it would be unwise to assume that all melanomas arise from a common cell, for some melanomas appear to be sarcomas and others carcinomas; but the same case may show changes entirely different. There are 6 excellent pathological illustrations.

Metastases simulating aneurysms

T. Lewis reports 2 cases of pulsating tumours over the upper part of the sternum, simulating pointing aneurysms, but in reality due to metastases from a hypernephroma. The patients, males aged 48 and 58 years, were syphilitic. The younger, who had been previously diagnosed as having an aortic aneurysm, had an enlarged right kidney, and a history of having had slight haematuria on two occasions. Later a radiogram showed an abnormal shadow above the level of the knob of the aorta, extending also above the level of the manubrium, and a clear picture of a metastasis in the upper part of the shaft of the left humerus. The older patient had tabes dorsalis, a blood pressure of 220/140, and occasionally red cells in the urine; he died in a uraemic condition. Necropsy showed a large hypernephroma of the upper pole of the right kidney; the aorta was much dilated, and a metastatic tumour spread from the manubrium. Emphasis is laid, as significant in these 2 cases, on the softness and slowness and a slight but just distinct delay in the rise of the pulse in such pulsating neoplasms.

Andrewes, F. W. (1898) *Trans. path. Soc. Lond.*, **49**, 259.

Broster, L. R. (1941) *Brit. med. J.*, **1**, 117.

Cleghorn, R. A. (1941) *Canad. med. Ass. J.*, **44**, 581.

Conybeare, J. J. (1941) *Brit. med. J.*, **1**, 688.

Friderichsen, C. (1918) *Jahrb. f. Kinderh.*, **87**, 109.

Greene, J. A., Levine, H., and Johnston, G. W. (1940) *Endocrinology*, **27**, 375.

Katz, F., and Mainzer, F. (1941) *Brit. med. J.*, **1**, 617.

are brought up, is more commonly a symptom of oesophagitis than of gastritis, the fluid collecting during the night in the oesophagus above the closed cardiac sphincter. Chronic alcoholic oesophagitis is a pre-cancerous condition. Whereas carcinoma of the stomach and colon is no commoner in males than in females, if allowance is made for the frequency of carcinoma of the mamma and uterus, this is not the case in the middle and lower parts of the oesophagus, where cancer is rare in women. The statistics of the Registrar-General for 1921 to 1923 showed that the death-rate for oesophageal carcinoma was more than four times greater in barmen, cellar-men, and waiters than in all men, and twenty times greater than in all ministers of religion.

Alcoholic beri-beri and vitamin B deficiency.—A. Hurst in discussing the results of alcoholism points out that it is doubtful if peripheral neuritis and cardiac failure ('beer heart') are ever due to excessive indulgence in alcohol alone. But deficiency of vitamin B causes the combination of peripheral neuritis with rapid pulse and cardiac failure which resembles beri-beri, and therefore is spoken of as alcoholic beri-beri or one of the non-tropical forms of beri-beri.

Gastritis.—Weak alcohol, such as beer, taken with meals has not any appreciable effect on the gastric mucosa; and strong alcoholic liquors, such as neat spirits and the stronger wines, have little, if any, effect on the stomach if taken in the course of a copious meal or soon after. But A. Hurst confirms the evil effects induced if alcohol is taken on an empty stomach, the first effect being inhibition of secretion of the gastric juice, this calling forth an abundant secretion of mucus; if alcoholism is continued, subacute gastritis follows. Unlike water, alcohol and any substances dissolved in it are absorbed by the stomach and so the damage to the gastric mucosa is increased, achlorhydria being a frequent result, and the chronic gastritis favours the onset of primary carcinoma of the stomach.

Pre-cirrhotic hepatitis.—A. Hurst explains that the pre-cirrhotic stage of hepatic cirrhosis is a toxic degeneration and therefore more accurately described as hepatosis rather than as hepatitis. It is commonly caused by alcohol, for example, in young men and girls who indulge in cocktails 3 or 4 times a week; this change is completely curable if abstinence is adopted, even if the habit has been persisted in for some months, for it is only when the indulgence has lasted for years that irreparable damage is done. The anxious parents are apt to ascribe the sallow complexion, loss of appetite, mental torpor, and irritability to some serious disease; the definite hepatic insufficiency, shown by the laevulose test, and the tender and often slightly enlarged liver rapidly disappear after a period of abstinence and rest with a light diet. Hurst ascribes 80 per cent of the cases of hepatic cirrhosis to alcoholism. Most of such patients have long lost their appetite and taste. Possibly other dietetic deficiencies also play a part in the causation of the cirrhosis; but it is not deficiency of vitamin B₁, because hepatic cirrhosis is seldom associated with either obvious or latent peripheral neuritis.

Colson, Z. W. (1940) *J. Amer. med. Ass.*, **115**, 1525.

Haggard, H. W., Greenberg, L. A., Carroll, R. P., and Miller, D. P. (1940) *J. Amer. med. Ass.*, **115**, 1680.

Hurst, A. (1940) *Brit. J. Ineb.*, **38**, 101.

Stevenson, L. D., McGowan, L. E., and Allen, A. M. (1941) *Arch. Neurol. Psychiat.*, *Chicago*, **45**, 56.

ALKALOSIS OCCURRING IN ALKALINE TREATMENT OF PEPTIC ULCER

See also B.E.M.P., Vol. I, p. 297; and Cumulative Supplement, Key No. 38.

Clinical Picture

Alkali poisoning in gastric ulcer

Excessive use of 'stomach powders'.—J. R. M. Whigham records the case of a man, aged 29 years, with a history of gastric ulcer for 5 years, who had acquired the habit of dosing himself with 'stomach powders' to relieve the pain. During the 3 months before admission to hospital the pain became constant and was not any longer relieved by the powders; he increased the self-treatment to 12 teaspoonful doses of the powder in the daytime and 2 during the night. As a result the vomiting got worse and the symptoms of ulcer became more obvious; further, mental deterioration, depression, drowsiness, fits, hiccup, and strangeness of manner supervened. After admission to hospital and some initial improvement, a severe attack of vomiting occurred, copious in amount, different in character from that previously noted, and somewhat suggesting pyloric obstruction. It seemed advisable to perform a rapid gastro-enterostomy for the gastric ulcer, the presence of which had meanwhile been confirmed. The patient made a good recovery. Before the operation the serum bicarbonate was about 70–80 per cent, the blood urea as high as 159 milligrams per 100 cubic centimetres, and the serum chlorides 242 per cent. The final figures were: serum bicarbonate 54 volumes per cent, blood urea 33 milligrams per 100 cubic centimetres, and the serum chloride 322 milligrams per cent.

Whigham, J. R. M. (1941) *Brit. J. Surg.*, **28**, 504.

ALLERGY

See also B.E.M.P., Vol. I, p. 302; Cumulative Supplement, Key Nos. 40–52; and Surveys and Abstracts 1939, p. 198; 1940, p. 159.

General Diagnosis of Allergic Cases and Identification Tests

Aetiology and pathology

Part played by histamine.—H. Goodman suggests the existence of a common activating agent which causes many different substances to present the same clinical picture. Thus histamine gives a clinical picture indistinguishable from that of the so-called allergic reaction, which is often traced to the application of certain cosmetics and coal-tar derivatives. It is further suggested that these responses occur when and if a toxic substance causes the formation of sufficient histamine to excite the symptoms associated with histamine poisoning.

Diagnosis

General investigation.—E. Yasuna in a review of the present opinions on allergy with regard to insulin, found 11 cases of generalized sensitivity to crystalline insulin, 3 cases of sensitivity to impurities contained in commercial insulin, and 12 cases suggesting sensitivity to insulin. Most of the subjects of this form of allergy were over 40 years of age with a history of allergy. All the patients showed skin manifestations, but only a few had circulatory or gastro-intestinal symptoms. Most of them had a history of a lapse in the therapy, with sensitivity occurring on resumption. In 3 cases the patients were successfully desensitized, and the others discontinued treatment. The author reports a case of generalized sensitivity to insulin confirmed by allergy studies.

Histaminase skin tests.—The suggestion that histamine is a mediator in allergic skin reactions and the tentative use of histaminase (an enzyme which destroys histamine) in clinical allergy, led H. Miller, R. C. Hawes, and G. Piness to investigate the problem experimentally. Skin reactions were measured by changes in the diameter of the wheals and flares before and after drug administration. No significant change in reaction could be observed as a result of histaminase injections given both orally and parenterally. No change was observed either in the reaction of passively sensitized sites to fish allergen. Although a slight alteration in sensitivity was observed in the case of grass allergens with histaminase, the results were not conclusive and may not have been specific to histaminase.

Treatment

Potassium chloride.—F. F. Furstenberg and L. N. Gay gave potassium chloride by mouth, in doses of 15 to 80 grains a day, to 85 allergic patients. These included 50 with hay fever, 17 with perennial allergic rhinitis, and the others were cases of rhinitis due to physical causes, angioneurotic oedema, urticaria, eczema, and bronchial asthma. The authors conclude that in the doses employed the drug had not proved of any value in the treatment of allergic diseases.

Allergic Diseases

Hay fever

Treatment by slow absorbing pollen extract.—The precipitation of the active element of pollen extract by tannic acid in order to slow down its absorption rate is described by H. L. Naterman. Two forms of precipitate were used: one was made by adding 0.5–1 per cent tannic acid to a dilute solution of pollen extract and suspended in Coca's buffered solution; the other was dried and kept as a powder. The supernatant liquid gave no scratch skin reactions, i.e. it did not contain any active element. One hundred and three patients were treated in two subsequent years; all had a high degree of sensitivity and moderately severe symptoms of various durations. Their ages and amount of previous treatment varied. Injections were made subcutaneously once or twice a week without any regular schedule, and the maximum dose repeated every 1 to 4 weeks until the beginning of the season and, in some cases, during the season. The hypo-sensitizing action of the extract was shown by a marked reduction in skin reactions in 46 out of 63 cases, a moderate reduction in 13 cases, and no reduction in 4 cases. Clinical results were satisfactory in 90 per cent of the patients, with an average total of 15 injections for each patient. The persistence of hypo-sensitization is indicated by greater tolerance in the second year of treatment, the smaller number of injections required, and relief even after a year without treatment. The advantages of the precipitate method are stability and absence of deterioration. It appears to have a greater de-sensitizing action, is more persistent and undergoes gradual dissociation and absorption after injection. Dissociation before injection may be prevented with zinc chloride. The active principle is concluded to be precipitable protein.

W. C. Spain, A. M. Fuchs, and Margaret B. Strauss describe the use of gelatin extract of ragweed pollen to prevent rapid absorption in injection therapy for hay fever. Its absorption rate was compared with that of aqueous extract by passive transfer tests on 8 non-sensitive adults, and was three times slower with gelatin extract. Ninety-five hay fever patients were divided into groups A, B, and C in order of sensitivity to both aqueous and gelatin extracts. Fifty-five were treated with gelatin extract during the season, on the usual aqueous extract schedule, rising to higher doses. The average tolerance of class C was 7,500 units in 14 injections, compared with 5,000 units in 18 aqueous injections. Class B took 4,400 units in 14 gelatin extracts and 2,500 units in 17 aqueous injections. Class A took 1,500 units in 13 gelatin injections and 500 units in 13 aqueous injections. Long intervals without injections do not necessitate a lower dosage on renewing the treatment, as in aqueous extracts. Forty persons were treated before the season with a new schedule of fewer injections and adapted to individual patients. The subjects in class C were given 5,000 units in 8 gelatin injections com-

pared with 18 aqueous injections; those in class B received 2,500 units in 8 gelatin injections compared with 17 aqueous injections; those in class A 500 units in 6 gelatin injections compared with 13 aqueous injections. Of those treated with the gelatin preparation 82.1 per cent were satisfactorily relieved as compared with 72.6 per cent of the aqueous controls. The patients selected for gelatin treatment were, moreover, those too sensitive for aqueous extracts. Constitutional reactions were few and there were not any local irritations. The preparation has the disadvantage of being difficult to liquefy and apt to produce delayed constitutional effects. The gelatin mixture must be carefully prepared and standardized according to the authors' recipe.

Oral pollen therapy.—S. M. Feinberg, F. L. Foran, M. R. Lichtenstein, E. Padnos, B. Z. Rappaport, J. Sheldon, and M. Zeller made a cooperative study of the use of oral pollen therapy in ragweed pollinosis. Their findings ranged from a complete rejection of the method to a limited acceptance. They agree with the opinion that, though in proper doses the method is safe, gastric reactions are frequent and troublesome but not dangerous, and that the efficacy of the therapy is at most little, especially in asthma, and definitely inferior to that obtainable by the parenteral injection of pollen extract.

Pollen extracts and skin sensitivity.—R. S. B. Pearson reports on his observations made to throw light on the contradictory accounts of the effects of injections of pollen extracts upon the cutaneous sensitivity of pollen-sensitive subjects. The main object was to determine if the cutaneous sensitivity was appreciably reduced by a series of injections of an increasing amount of such extracts in hay fever patients and, if so, to what extent and for how long. The following conclusions are the result of work carried out on 8 patients for 3 years and on 3 others for 2 years: (1) injection of graded doses of pollen extract up to 100,000 units is accompanied in most cases by a slight diminution of skin sensitivity, as shown by the intradermal test, and a well-marked diminution with the scratch test; (2) such skin desensitization as occurs is temporary and is no greater after 3 successive years of treatment than after one; (3) a local area of more complete desensitization occurs at the site of weekly injections of extract than in the skin elsewhere; (4) there was not any evidence in support of the view that injection of individual pollen extracts leads to specific desensitization to the pollens in question and not to other species of grass pollen.

Effect of pollen contact on the age of onset.—J. A. Clarke, Jun. and H. C. Leopold compared two groups of patients with hay fever; members of one group were born in America, and members of the second were born in Europe. The European-born patients required the same 'incubation period' after the first contact with ragweed pollen, regardless of their age at the time of first contact. The concentration of the exposure may also be a factor; in support of this is the larger number of male sufferers in the first decade of life. Exposure to substances other than pollen, such as house dust and orris root, may account for poor results of specific treatment, particularly in women.

Allergy of the skin

Allergic eczema and cataract.—J. G. Milner records the case of a man, aged 26, who for many years had been subject to attacks of allergic eczema; for 5 years the eyelids and eyebrows had been involved. He had also suffered from asthma and colitis. His father had had similar allergic manifestations but not eczema. In February 1940 the son was found to have an anterior cataract. A review of the association of skin diseases and cataract shows that this has been recognized since 1868 by Rothmund, whose cases have been regarded by E. Grönbläd as probably poikiloderma Jakobi, a rare disease which may be associated with cataract. Milner regards the cataract as being directly associated with allergic eczema. The lens, though like the conjunctiva and the superficial layers of the cornea, ectodermal in origin, is very rarely involved in skin diseases. The association of tetany (parathyroid insufficiency) with cataract is well known, and some have thought that the cataract accompanying skin diseases may also be due to parathyroid dysfunction, but there does not seem to be enough evidence in support of this.

Infantile eczema.—L. W. Hill reports on the use of amino-acids as a source of nitrogen food in 36 infants allergic to milk. The proportion used had the following composition: amino-acids, 20 per cent, dextri-maltose 42.3 per cent, virgin olive oil 18 per cent, arrowroot starch 10 per cent, brewers' yeast powder 3 per cent, and mineral salts 6.7 per cent; one level tablespoonful of this powder contains 35 calories. In 19 cases the food was taken well by the baby, improved the eczema, and caused satisfactory gains in weight. In 9 cases it caused either diarrhoea or vomiting, was taken either poorly or not at all, or caused unsatisfactory gains in weight. In the other 8 cases the results were inconclusive.

Caused by fungous disease.—According to P. Schonwald many cases of skin allergy are due to fungous infection, particularly trichophytosis and epidermophytosis. Most of these fungous allergy cases are complicated by sensitization to other allergens. Success in treatment can be obtained only by proper elimination with or without desensitization to all appropriate allergens. Patients with uncomplicated fungous allergy can obtain prompt and lasting relief when treated with the proper fungus extract.

Treatment by histaminase.—L. C. Goldberg employed histaminase in 35 cases of various allergic dermatoses, such as chronic urticaria, dermatographism, eczema, and idiopathic pruritus. In 25 cases the drug was given by mouth, and in 10 cases by intramuscular injection, 2 cubic centimetres of solution being given every other day in from 6 to 12 injections. In all

but 9 of the cases there was partial or total improvement. As much as 150 histamine detoxicating units were given daily for 4 or 5 days without any untoward reactions. The unit is the amount necessary to inactivate 1 milligram of histamine during 24 hours' incubation at 37° C. in a phosphate buffer solution at a hydrogen ion concentration of 7.

Gastro-intestinal allergy

Milk as a cause.—L. Cardon claims that food allergy is a more common cause of functional intestinal disturbance and spastic colon than is generally appreciated. Milk is one of the more common allergens responsible for such colonic food allergy, accounting for 25 per cent of cases. Milk allergy can be more readily recognized or excluded by the simple trial and error method than other common food allergens, because it is more easily eliminated from the diet. The length of the period after a single intake of milk before symptoms appear is variable and inversely proportional to the degree of sensitivity and the amount of milk consumed; symptoms may appear within a few minutes, or may be delayed for 12 to 24 hours. The duration of symptoms after a single ingestion also varies, and is directly proportional to the degree of sensitivity and the amount of allergen ingested; it may vary from 1 to 24 or 36 hours. A symptom-free interval, in the period between rising in the morning and taking breakfast, often occurs and is important in the diagnosis of food allergy.

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AMOEBIASIS

See also B.E.M.P., Vol. I, p. 366; Cumulative Supplement, Key No. 56; and Surveys and Abstracts 1940, p. 167.

Amoebic Dysentery

Clinical picture

Amoebiasis cutis.—T. E. Wyatt and R. R. Buchholz report 2 cases of gangrene and ulceration of the skin of the anterior abdominal wall due to infestation with the *Entamoeba histolytica*. Amoebiasis cutis is a rare manifestation of amoebiasis, the authors having been able to collect from only 28 published and authentic cases of amoebiasis of the skin associated with visceral lesions. Of these patients 15 recovered, 11 died, and it was impossible to obtain further information about 2 cases. One of the authors' patients was an elderly negress who developed gangrene of the skin after drainage of a liver abscess. Emetine hydrochloride was given in doses of 0.03 gramme twice daily, and an extensive debridement performed, but the patient died on the fifteenth post-operative day. The other case reported was that of a man, aged 34, in whom also developed an extensive gangrene and ulceration of the abdominal wall after drainage of a liver abscess. On the seventh day in hospital motile forms of *Entamoeba histolytica* were found, and he was given emetine hydrochloride, in a dosage of 0.065 gramme intramuscularly each day for 12 days. Extensive débridement of old devitalized tissue was also performed. The wound granulated, and skin grafts were applied. The patient was discharged perfectly well. The authors emphasize the importance of early administration of emetine, and of extensive debridement in such cases.

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AMYLOID DISEASE

See also B.E.M.P., Vol. I, p. 401; and Cumulative Supplement, Key No. 58.

Clinical Picture

General symptomatology

Increasing rarity.—In a recent number of studies from the Institute of Pathology, Belfast, there is, over the initials 'A. R. C.', an account with commentary of the case of a woman, aged 34 years, with amyloid disease of the kidneys, spleen, liver, adrenals, lungs, thyroid, and vascular system. The case presents some features of interest. The increasing rarity of amyloid infiltration is exemplified in the last 2,000 necropsies, in which there were 2 other cases, one due to osteomyelitis of the femur for 10 years, the other with bilateral apical bronchiectasis of tuberculous origin. In the present case none of the recognized aetiological conditions was found clinically or at the necropsy. The lungs, in addition to emphysema, showed a peculiar patchy calcification of the alveolar walls with fibrosis and a layer of amyloid

material just under the alveolar epithelium. Calcification in the pulmonary veins and renal and coronary arteries suggests some undiscovered disturbance in calcium metabolism, but no lesion was found in the parathyroids. The adrenals showed extensive infiltration of the cortex, the zona fasciculata and the zona reticulata being almost entirely replaced by amyloid; the zona glomerulosa was relatively normal.

'A. R. C.' (1941) *Ulster med. J.*, 10, 68.

ANAEMIA

See also B.E.M.P., Vol. I, p. 408; Cumulative Supplement, Key No. 59; and Surveys and Abstracts 1939, pp. 53 and 203; 1940, pp. 32 and 168.

Pernicious Anaemia

Aetiology

Vitamin K plasma-prothrombin relation.—J. W. Lord, Jun., W. DeW. Andrus, and R. A. Moore compare the factors, the derangement of which results in pernicious anaemia, and the vitamin K plasma-prothrombin relation. These two entities are similar physiologically and anatomically. Prothrombin is continuously disappearing from the circulating blood, and experiments point to the lung as the site of the loss. The critical level of the plasma prothrombin is approximately 20 per cent of normal.

Treatment

Erythrocyte response in the blood.—The value of the reticulocyte count as an indication of the response to treatment in pernicious anaemia is questioned by M. C. Riddle. He admits the efficacy of this method of assaying therapeutic agents and in regulating their dosage and in estimating dosage required for any one patient, but as an indication of the final prognosis, prefers to use the erythrocyte response, i.e. the increase in the erythrocyte count. His observations were made on 600 patients with pernicious anaemia, in 597 of whom remissions occurred; 114 patients received liver extract orally; 149 received ventriculin; 85 received liver extract intramuscularly, and 175 intravenously; and the remaining 74 patients either had spontaneous remissions or had other forms of treatment. Riddle states that the average weekly increase in the erythrocyte count for 349 patients indicated that they were 'satisfactorily treated' and for 174 patients that they were 'unsatisfactorily treated'. The rise in the erythrocyte count is more rapid at first and slower towards the end of the remission, and at the end of 2 weeks is inversely related to the original erythrocyte count. Data at the end of the first 2 weeks of treatment have provided a standard equation which can be used as a standard for the relative efficacy of any kind of treatment in patients with pernicious anaemia. If the patient's erythrocyte count reaches this standard, it indicates that the erythrocyte count will reach about 4.5 millions per cubic millimetre in between 6 and 8 weeks of treatment. Patients whose count does not reach this standard are being inadequately treated and may be expected to have a final erythrocyte count less than 4.5 millions. The equation obtained by Riddle is $I = 0.78 - 0.174E_o$, in which I is the average weekly increase in the erythrocyte count during the first 2 weeks of treatment, and E_o the erythrocyte count before treatment in millions per cubic millimetre of blood. Complicating factors in the disease invalidate the accuracy of this standard. Riddle discusses the comparative values of the reticulocyte response and the erythrocyte response and the particular advantages and disadvantages of each.

Hypochromic Deficiency Anaemias

Chlorosis

G. Alsted reports 6 cases of chlorosis in young women, the only cases observed during a 10-year period at the Frederiksberg Hospital, Copenhagen. The age distribution of the patients was somewhat higher than that found in earlier series of cases; also menstrual disturbances seemed to be rarer than generally reported. All the patients were from a social class which suggested that their diets had been quantitatively insufficient, and two-thirds were admitted to hospital during the darkest period of the year, suggesting a qualitative deficiency. All responded well to iron treatment. The disease thus appears not to have entirely disappeared. The author suggests the term *essential juvenile iron deficiency* for the condition.

Anaemias Due to Blood Loss

Acute haemorrhage

Biochemistry of blood in gastro-intestinal cases.—B. Johnson noted a marked rise in the non-protein and urea nitrogen of the blood in cases of severe upper gastro-intestinal haemorrhages only when there was a temporary or permanent reduction in renal function. The duration of the azotaemia was from 3 to 5 days after a single haemorrhage, but was more prolonged when there were repeated haemorrhages. Changes were not noted in the serum chloride or in the plasma carbon dioxide combining power. Whole blood in the upper gastro-intestinal tract is digested and absorbed, and results in the formation of urea. The pathogenesis of the azotaemia depends on a rate of urea formation which is in excess of the rate at which urea can be excreted by the kidneys. Definite correlation between the degree of azotaemia and the prognosis for recovery was not found.

Haemolytic Anaemias

Familial crisis

W. Dameshek reports on three children in the same household—two brothers and a cousin—who, within a period of 10 days, were admitted to hospital with severe haemolytic crises.

Splenectomy was performed on all three, with one death, the other two making uneventful recoveries. It was considered possible that these haemolytic crises developed because of some alteration outside the bone marrow, perhaps as a result of splenic activation.

Clinical picture

Cooley's erythroblastic anaemia.—B. J. Wood records a case, the first recognized at the Mayo Clinic, of Cooley's, or erythroblastic, anaemia which has been found exclusively among children of Mediterranean ancestry, especially Greeks, and occurs in the first decade of life, most often in the first two years. The chief signs are pallor and progressive enlargement of the abdomen with considerable smooth splenomegaly and some increase in the size of the liver. When the disease begins in the first year of life physical growth is usually retarded, but mentality is not involved. The patients closely resemble each other and present a mongoloid appearance. Radiologically the bones show prominent trabeculations in the medulla, most prominent in the metacarpal and metatarsal bones, causing definite widening of the bones, the cortex being thin and occasionally containing punched-out areas. In earlier stages or in milder cases the skull shows osteoporosis and thinning of the tables. In advanced stages the outer table is so thin and porous that it cannot be detected as a distinct layer of bone; the diploë are prominent and appear radiologically to extend beyond the outer table as spicules of bone, and have been compared to 'hair standing on end'. These radiological appearances are also present in sickle-celled anaemia and in familial haemolytic jaundice. The red blood count ranges from 1 to 4 millions, the colour index is less than 1, with the leucocyte count from 10,000 to 50,000. Megaloblasts, erythroblasts, and Howell-Jolly bodies may be present, and reticulated erythrocytes may constitute 10 to 30 per cent of the total red count. Patients seldom live to adult life, as the course is steadily downhill without spontaneous remissions or exacerbations. Benefit from blood transfusions is only temporary. Death is often due to secondary infection or to acute dilatation of the heart. J. D. Camp points out that, though the disease is commonly thought to occur in children of Mediterranean parentage, radiological examination of the skulls of pre-Columbian Peruvians and the skeletons of Arkansas mound-builders show changes identical to those seen in cases of erythroblastic anaemia.

Acute or subacute haemolytic anaemia (Lederer)

Erythrophagocytic anaemia.—M. M. Hargraves, W. E. Herrell, and R. O. Pearman report, under the heading erythrophagocytic anaemia (Lederer's anaemia?), a case with recovery: a man aged 54, who since 1914 had been subject to exacerbations of a urinary infection. In December 1938 a calculus was removed from the right ureter without any immediate untoward results; but about a week later he became acutely ill with abdominal pain, nausea, vomiting, and progressive jaundice, and gave a direct van den Bergh reaction. The blood picture showed anaemia (1,860,000), haemoglobin 5 grammes, remarkable phagocytosis of the red cells by monocytes, macrophages and polymorphonuclears, and anisocytosis with considerable increase in regeneration, but not the generalized spherical microcytosis of the erythrocytes seen in familial haemolytic jaundice. Many red cells were actually drawn out into a pear or funnel shape as if pulled into leucocytes. The patient continued severely ill with shock, cyanosis, fever (104° F.), pulse 140, respirations 40, until after transfusion; he was given daily 500 cubic centimetres of citrated blood followed by 500 cubic centimetres of 20 per cent solution of glucose. Within 24 hours the phagocytosis ceased, and within 5 days the leucocyte count, which had been 30,200, touched normal levels. The extraordinary amount of erythrophagocytosis was undoubtedly the active mechanism responsible for the rapid haemolysis, and the donor's blood evidently supplied the antidotal substance needed. The authors conclude that it is a question whether this unique case should be regarded as a distinct entity, namely erythrophagocytic anaemia, or whether it shows the mechanism of haemolysis, not hitherto reported, in Lederer's anaemia. Erythrophagocytosis has been recorded in sub-acute bacterial endocarditis, in crises of congenital haemolytic jaundice, in the therapeutic inoculation of malaria, and in anaemia of the new-born.

'Baghdad spring anaemia.'—R. Lederer reports a new form of acute haemolytic anaemia in Baghdad, during only a few weeks of spring. The disease runs a rapid course—the only fatal case lasted 36 hours—and has a mortality of 10 per cent; it is curable by injection or transfusion of blood, liver therapy in large doses, and adrenaline. Only boys, especially Jews, of a significant constitutional type are affected. The anaemia is an anaphylactic reaction to contact with flowers and young fruit. The author suggests the name 'Baghdad spring anaemia' for this disease.

Chronic haemolytic anaemia with haemoglobinuria

G. C. Ham and H. M. Horack report on a case of chronic haemolytic anaemia with paroxysmal nocturnal haemoglobinuria (Marchiafava-Micheli syndrome); but in this case the usual nocturnal haemoglobinuria was infrequent. The patient was a woman of 46. Splenectomy did not influence the course or degree of the anaemia, but it reduced the frequency and severity of the haemoglobinuria. At necropsy little was found other than the usual multiple vascular thrombi and histopathological changes which could be attributed to the prolonged haemoglobinuria.

Haemolytic Anaemias of the New-born

Icterus gravis neonatorum

Erythroblastosis.—Helen McKinley reviews the subject of icterus gravis neonatorum with

erythroblastosis, a wide-spread extra-medullary haematopoiesis, especially in the liver and spleen. Erythroblastæmia is defined as the presence in the peripheral circulation of nucleated red blood cells in larger numbers than the physiological maximum for the age, and is regarded as a definite disease. There are three very closely related conditions: (1) hydrops foetalis, (2) haemolytic anaemia, and (3) icterus gravis neonatorum. The escape of the two eldest children in a family may obscure the hereditary and familial histories. The 'kernikterus' (nuclear jaundice) lesions in the nervous system are in the striato-pallidal region. From 1930 to 1939 there were 37 cases of icterus gravis neonatorum admitted to the hospital at Toronto and of these 20, or 54 per cent, proved fatal; in 11 of the survivors there was complete recovery. Up to 1935 the treatment consisted in repeated blood transfusions; then calcium gluconate was introduced and in 1936 liver extract was given intramuscularly. The combination of these three remedies has been extremely effective.

Hepatic changes.—W. W. Zuelzer and J. A. Bigler describe hepatic changes in 2 cases of familial icterus gravis neonatorum. In one case, fatal at the age of 8 months, there was cirrhosis. The other infant died of kernikterus at the end of the first week of life. Severe fatty changes, haemosiderosis, and deposits of bile pigment were found in the liver. There was not any clinical or pathological evidence of erythroblastosis in either case.

Vitamin K treatment.—Evelyn W. Mayman reports a case of erythroblastosis (icterus gravis neonatorum). Twelve hours after the injection of 4 cubic centimetres of vitamin K, the stools and urine became very yellow. Further doses of vitamin K were given and, by the eighteenth post-natal day, jaundice was definitely less. The infant made a good recovery.

Aplastic Anaemia

Idiopathic aplastic anaemia

Treatment by intrasternal introduction of bone marrow.—M. Morrison and A. A. Samwick make a preliminary report on the use of human bone marrow introduced intrasternally in a case of idiopathic aplastic anaemia. The patient's haemoglobin content was 58 per cent, red blood cell count 2,640,000, leucocytes count 2,300, platelets diminished to absent, a bleeding time of 6½ minutes, and a coagulation time of 2 minutes. A bone marrow aspiration was performed on the patient and the needle with the solid obturator in it was left *in situ*. Three cubic centimetres of bone marrow were withdrawn from the patient's brother (group O) and immediately injected into the patient's sternal marrow. Next day another 5 cubic centimetres of bone marrow were given. On the following day 5 cubic centimetres of bone marrow from another donor were given. The patient gradually improved, and 40 days later the haemoglobin percentage was 73 per cent, the red blood cell count 5,000,000, the leucocyte count 7,000, and the platelets adequate.

Acholic Jaundice

Familial non-haemolytic jaundice

Differential diagnosis.—W. Dameshek and K. Singer describe their observations on two families (and in a postscript refer to a third family) with chronic, usually mild, non-haemolytic, non-obstructive, acholic retention jaundice which is regarded as due to constitutional hepatic dysfunction with an indirect van den Bergh reaction. Although superficially the disease in these families resembled the mild or latent cases of the well-established congenital or familial haemolytic (acholic) jaundice, evidence is brought forward to show that the presence of haemolysis can be excluded and that an indirect van den Bergh reaction does not necessarily indicate a haemolytic process. Two aspects of the problem are important: (1) Is it certain that familial non-haemolytic jaundice can be regarded as a well-defined syndrome to be clearly distinguished from familial haemolytic jaundice and chronic mild hepatic disease, and (2) if so, what are the possible pathological mechanisms involved? The differences between the characteristics of the two forms are tabulated; thus in the familial non-haemolytic families reported there was absence of positive evidence of the following features of familial haemolytic jaundice: splenomegaly, spherocytosis, reticulocytosis, increased fragility to sodium chloride and lysolecithin, and hyperactivity of the bone marrow. Haemolytic jaundice was further ruled out by the normal or even somewhat low value of the daily output of urobilinogen in the faeces. The hereditary nature of the non-haemolytic jaundice and its long duration without symptoms or signs of progressive hepatic disease indicate a simple functional disorder of the liver such as an alteration in the permeability of the liver cells which retards the excretion of bilirubin.

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ANAESTHESIA

See also B.E.M.P., Vol. I, p. 472; Cumulative Supplement, Key No. 60; and Surveys and Abstracts 1939, pp. 25, 163, and 207; 1940, pp. 108 and 172.

Spinal Anaesthesia

Technique

Neosynephrin for maintaining blood pressure.—H. I. Silvers and I. E. Leonard, Jun., claim that neosynephrin (*l*- α -hydroxy- β -methyl-amino-3-hydroxyethylbenzene hydrochloride) is effective in maintenance of the stability of blood pressure during spinal anaesthesia. After its administration there is bradycardia. In therapeutic doses untoward effects such as arrhythmia, palpitation, anxiety, or nervousness do not occur. The drug was mixed with 1 per cent novocain (procaine hydrochloride) and given subcutaneously and intramuscularly over the site chosen for the spinal puncture. The initial dosage was 0.5 cubic centimetre of 1 per cent neosynephrin hydrochloride. Administration of the spinal anaesthetic occupied 5 to 10 minutes. The blood pressure and pulse were taken when the patient reached the operating theatre, immediately after the spinal anaesthetic had been given, and every 5 minutes thereafter. The average rise in blood pressure, approximately 20 points, occurred 10 to 15 minutes after injection of the drug, and lasted 25 to 30 minutes. The average blood pressure was higher during the operation than the average normal blood pressure pre-operatively. In only 10 out of 50 cases was the drug repeated during the operation.

Local Anaesthesia

Local injection

Procaine hydrochloride.—J. S. Lundy, E. B. Tuohy, R. C. Adams, and L. H. Mousel regard procaine hydrochloride (novocain, neocaine) as the most valuable among all local anaesthetics, because it seldom gives rise to untoward symptoms. Another local anaesthetic, metycaine hydrochloride, may be a satisfactory substitute for procaine, and produces local, topical, regional, and spinal anaesthesia of longer duration than do equivalent doses of procaine. Some vasoconstrictors, such as epinephrine, cobefrin, and neosynephrin, are used in combination with the above anaesthetics in order to produce a more lasting effect and to prevent rapid absorption of the local anaesthetic; they also serve as haemostatics. The administration of a combination of rapidly acting soluble barbiturates, such as pentothal sodium and evipan soluble, is often useful in minimizing the risk of operation in some patients. A regional block of the abdominal wall with a local anaesthetic combined with intravenous anaesthesia induced by pentothal sodium will often allow laparotomy to be performed with the least possible inconvenience to the patient.

Rectal Anaesthesia and Basal Narcosis

Technique

Avertin.—R. C. Romig and C. D. Donahue, finding that little had been published about the use of avertin in patients of advanced age, reviewed 200 cases in which the drug was employed as a basal anaesthetic without any fatality attributable to the anaesthetic. The youngest patient was aged 50, and the oldest 86; 10 in the eighth decade were anaesthetized safely. Of the patients, 18 were subjected to more than one anaesthesia. Most of the patients underwent major operations. There were 179 resections, 4 prostatectomies, 4 hydroceles, 5 lithotripsies, 5 dilatations of the posterior or anterior urethra, 2 cystotomies, 1 nephrostomy, 20 biopsies or post-operative bleeding or instrumentation, 2 epididymectomies, 1 nephrectomy, 1 carcinoma of the urethra in a female, making a total of 224 operations or instrumentations on 200 patients. In 19 patients, most of whom had undergone major operations, serious respiratory or cardiac failure occurred. The authors consider that the incidence of these sequelae would have been less if the pre-operative injection of opiates, which all but 2 of the patients received, had not been given. According to the authors the decided advantages of avertin anaesthesia are the absence of psychic trauma, marked decrease in post-operative vomiting, the early intake of fluids and food by mouth, and the willingness of the patient to have further anaesthetics.

Basal narcosis

Hexobarbitone soluble (evipan sodium).—F. K. Boston and N. R. James report on the use of hexobarbitone soluble (evipan sodium) rectally as a pre-anaesthetic basal hypnotic on more than 250 patients undergoing various surgical procedures. The dosage was estimated by multiplying the patient's weight in pounds by 0.02. There was generally complete amnesia during transit to and from the operating theatre and for some hours afterwards. The authors consider that the use of this drug is a satisfactory and easy means of producing basal narcosis.

Blood-oxygen capacity after hexobarbitone soluble.—E. A. Pask investigated the blood-oxygen capacity directly in a short series of patients after soluble hexobarbitone anaesthesia. The small reduction in oxygen capacity noted in some of the cases reported here cannot be

regarded as significant, and it may be concluded that a serious fall in blood-oxygen capacity is not a common accompaniment of clinical soluble hexobarbitone anaesthesia in man.

Intravenous administration.—The use of intravenous anaesthesia has, as J. S. Lundy, E. B. Tuohy, R. C. Adams, and L. H. Mousel point out, steadily increased and proved of value in some conditions and operations in which it was formerly regarded as contra-indicated. Pentothal sodium continues to be the preferable anaesthetic, and evipan sodium, which has a similar short action, is also used. The one outstanding and definite contra-indication to intravenous anaesthesia is a cardiac condition with advanced myocardial disease, especially if associated with dyspnoea; but the authors do not consider pentothal sodium to be a satisfactory anaesthetic for young children. This drug appears to be rapidly destroyed in the body, and traces of its degradation products have been difficult to isolate from the urine. It has been assumed that pentothal sodium, like its oxygen homologue, pentobarbital sodium, is detoxified in the liver and that therefore pentothal sodium is a dangerous anaesthetic for patients with hepatic disease. But both clinically and experimentally this now appears to have been a misconception, and the presence of hepatic or renal disease is not a contra-indication, though a reason for care. The scope and safety of intravenous anaesthesia have been increased by the simultaneous administration of oxygen or 50 per cent oxygen with 50 per cent nitrous oxide. It is much used for the induction for other forms of general anaesthesia and to supplement spinal, local, and regional anaesthesia.

Pre-Anaesthetic Sedatives

Opium

As a sedative for children.—A. H. L. Baker and E. M. Chivers state that opium derivatives are well tolerated by children; they found that morphine or hyoscine, or omnopon and hyoscine, in appropriate doses were satisfactory as pre-anaesthetic sedatives in 600 children between the ages of 1 month and 16 years. The dosage was found to depend on the basal metabolic rate, which increases to a maximum at the age of 6 years, declines up to 12, rises again during puberty, and then declines throughout life.

Baker, A. H. L., and Chivers, E. M. (1941) *Lancet*, **1**, 171.

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Lundy, J. S., Tuohy, E. B., Adams, R. C., and Mousel, L. H. (1941) *Proc. Mayo Clin.*, **16**, 78.

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Romig, R. C., and Donahue, C. D. (1941) *Northw. Med., Seattle*, **40**, 37.

Silvers, H. I., Leonard, I. E., Jun. (1940) *Amer. J. Surg.*, **50**, 79.

ANEURYSM

See also B.E.M.P., Vol. I, p. 501; Cumulative Supplement, Key No. 61; and Surveys and Abstracts 1939, p. 213; 1940, p. 179.

Aneurysm of the Aorta (Thoracic and Abdominal)

Clinical picture

Aneurysm of the abdominal aorta.—G. H. Jennings reports 4 cases of abdominal aneurysm in 2 of which a syphilitic aetiology was possible. Symptoms included backache, sciatica, testicular pain, malaena, constipation, abdominal cramp, suppression of urine, and those of intestinal obstruction. In 3 of the cases there was an expansile pulsating abdominal tumour. Spinal radiography and a Wassermann test assisted the diagnosis in one case. The course from diagnosis to death by retroperitoneal rupture was 9 days in the first case, and about 10 weeks in the second and third. Necropsy showed evidence of previous smaller bleedings in all cases.

Aortic aneurysm and pulmonary stenosis.—K. L. Dickens records the case of a syphilitic negro woman, aged 28, with the clinical and radiological pictures of aneurysm of the pulmonary artery with stenosis and insufficiency of the pulmonary orifice. Necropsy showed an aneurysm arising from the region of the aortic sinuses of Valsalva, just above the junction of the right and left anterior cusps of the aortic valve. This aneurysm herniated into the pulmonary artery, which in its turn protruded into the right ventricle, the combined pressure and anatomical distortion causing stenosis of the pulmonary artery. The aneurysmal sac also caused distortion of the right posterior cusp of the pulmonary valve so that it could not be recognized as such and appeared merely as a thin rim of tissue. The situation of the aneurysm was very unusual, as were its ultimate effects on the pulmonary system.

Aneurysm of the coeliac artery

With symptoms of acute cholecystitis.—A. D. Le Vay records a case in a widow, aged 58, of rupture of an aneurysm of the coeliac artery into the lesser sac of the peritoneum. This extremely rare aneurysm has been previously reported on 2 occasions only. There was not any evidence of syphilis and there was very little general arteriosclerosis. The aneurysm was large with a diameter of 3 or 4 inches, compressing the common bile duct and causing jaundice, and the inferior vena and causing ante-mortem clot, some of which had passed into the pulmonary artery. There was recent infarction of both lower lobes of the lungs. The clinical picture was that of acute cholecystitis with regional peritonitis.

Aneurysm of the abdominal aorta

Diagnosis.—C. A. W. Uhle, in a discussion of the significance of aneurysm of the abdominal

aorta masquerading as primary urological disease, emphasizes the importance of the fundamental consideration of the history and physical examination. Cases may simulate perinephric abscess, renal lithiasis, hydronephrosis, renal tumour, and perirenal haemorrhage. Haematuria, uraemia, and anuria have been confusing elements in the symptomatology. The physical findings require confirmation or additional diagnostic aid from cystoscopic and X-ray examinations. Erosion of the vertebral bodies should be looked for in every suspected case.

Dissecting Aneurysm

Secondary to renal calcification

S. Mayer, Jun., reports a case in which severe hypertension developed some years after the diagnosis of hyperparathyroidism, presumably largely due to severe changes in the kidneys secondary to calcification. A dissecting aneurysm of the aorta and right renal artery, diagnosed during life, occurred. The aneurysm was apparently the result of the coincidence of an atheromatous weakened aortic wall, and increased intra-aortic stress due to the increased blood pressure. In the end it ruptured and caused death.

Aneurysm of the Pulmonary Artery

Clinical picture

Congenital defect in a child.—K. D. Wilkinson records a case of aneurysmal dilatation of the pulmonary artery in a girl who was regarded as normal until the age of 10 years, and died suddenly three years later from rupture of the pulmonary aneurysm into the pericardium. A long systolic murmur was audible at the base, loudest in the left second interspace, and the second sound was clear and loud. The electrocardiogram showed a low voltage in lead I with a tall R2 and R3 and a P-R interval of 0.16 of a second. Necropsy showed enormous distension of the pericardium with fluid blood and so much enlargement of the heart that the left lung was much compressed. The pulmonary artery measured 3 inches in diameter; its valves, two in number, were comparatively large but normal in texture. About 1 inch above the valve there was a linear split, 2 inches in length and perforating at one point into the pericardium. The aortic, mitral, and tricuspid valves were normal. The author points out that when aneurysm of the pulmonary artery is the result of congenital defect it is usually associated with a patent interauricular septum; here this was not the case.

Peripheral Aneurysm

Aneurysm of the internal carotid

Causing aural haemorrhage.—N. Young reports 2 cases of copious bleeding from the ear. In one case certainly, and in the other probably, the blood escaped in the first place through the wall of the cervical portion of the internal carotid artery, into the para-pharyngeal space, and thence tracked along a well defined anatomical path into the parotid space, and so through the wall of the auditory meatus. The author suggests that profuse unheralded aural haemorrhage is more often due to erosion of the extracranial than of the intracranial portion of the internal carotid artery. These haemorrhages from the ear occur only in cases of erosive aneurysm, and almost always in children. With regard to treatment, some form of carotid occlusion is generally indicated, but incision of the pharyngeal swelling should be avoided, and any drainage should be to the surface of the neck.

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Le Vay, A. D. (1941) *Brit. J. Surg.*, 28, 502.

Mayer, S., Jun. (1941) *Johns Hopk. Hosp. Bull.*, 68, 319.

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Wilkinson, K. D. (1940) *Brit. Heart J.*, 2, 255.

Young, N. (1941) *J. Laryng.*, 56, 35.

ANGINA PECTORIS AND CORONARY THROMBOSIS

See also B.E.M.P., Vol. I, p. 547; Cumulative Supplement, Key No. 62; and Surveys and Abstracts 1939, p. 215; 1940, p. 181.

Angina Pectoris

Pathology and pathogenesis of anginal pain

Coronary artery rupture.—J. Mackay reports a case of coronary haemorrhage in a woman, aged 62, in which there was an unusually long period between the first sign of distress and death. The first symptom was vomiting of bile-stained fluid. The next day she had a tight sensation in the epigastrium and 2 days later she complained of severe pain in the epigastrium, and almost collapsed. The next morning she was comparatively comfortable, but later in the day collapsed and died. At necropsy the pericardial sac was full of clotted blood. There was an area of ecchymosis over the anterior branch of the left coronary artery, and fragmentation of muscle in the centre of this area. There was rupture of an underlying vessel; but no infarcts or thrombosis could be found.

Treatment

Aminophylline.—G. V. Le Roy gave aminophylline (theophylline with ethylenediamine) or placebos in varying amounts to 68 patients with angina pectoris during a period of 2 years. Though approximately 20 per cent of the patients stated that placebos and sedative drugs were beneficial, about 75 per cent reported definite benefit from the use of theophylline with ethylenediamine. When the drug was replaced by placebos or withdrawn from the patients

who had benefited from the use of theophylline with ethylenediamine, the symptoms recurred within less than 3 months in about 80 per cent. The dosage of the drug was not less than 0.2 gramme 3 times daily, and in some cases as much as 0.8 to 1.0 gramme daily was given. Of the 68 patients, 39, or 57 per cent, were less than 50 years of age, and only 5 were more than 60 years of age. With regard to the benefit obtained from the use of the drug, in some cases this amounted to complete freedom from pain, but usually the patient reported a definite diminution in the incidence and severity of attacks, without complete freedom from pain, but as a rule requiring more exertion or excitement to provoke an attack than before the use of the drug, and when an attack did occur it was milder and passed off more quickly.

Coronary Thrombosis

Clinical picture

Character of prodromal pain.—B. Blumenthal and J. A. Reisinger, on the basis of histories obtained from 32 patients, state that the prodromal attacks of pain in coronary occlusion vary greatly in duration, character, and length of the period by which they precede the obvious manifestations of coronary occlusion. Generally the pain appears suddenly, without obvious precipitating causes, when the patient is apparently in good health, and it varies in duration from 15 minutes to hours, and from a mild ache to extreme severity. It is generally referred to the anterior chest wall between the midclavicular lines. The mechanism responsible for the pain is obscure, but intramural haemorrhage may be an important factor.

Coronary occlusion.—From analysis of the histories of 260 cases of acute coronary occlusion A. M. Master, S. Dack, and H. L. Jaffe find that premonitory symptoms occurred in 44.2 per cent. In most cases these consist of substernal or precordial pain or discomfort. Some patients experienced fatigue, weakness, gastric distress, dyspnoea, palpitation, nervousness, and dizziness. The sudden appearance of a typical anginal syndrome or the sudden acceleration of a pre-existing anginal syndrome often preceded evidence of occlusion. The premonitory symptoms often appeared within 24 hours before the acute attack, but in some cases they began 2 or 3 weeks before. The duration of the symptoms varied from a few minutes to several hours.

M. G. Nelson analyses the records of 121 cases of coronary occlusion admitted during 12 years to the Royal Victoria Hospital, Belfast. This title is regarded as more satisfactory than 'coronary thrombosis' and 'cardiac infarction', often used as synonymous, but which are really more definite and cannot be accurately diagnosed clinically. Except for the rare accident of coronary embolism, coronary occlusion seldom occurs except in cases with coronary disease, and the important disposing condition is atherosclerosis of the coronaries. Three phases are described: (1) coronary atherosclerosis, in 15 per cent of which there are not any symptoms, but in those with symptoms, angina of effort occurred in 53 per cent, dyspnoea on exertion in 42 per cent, previous occlusion in 30 per cent, 'indigestion' in 17 per cent, and cardiac asthma in 9 per cent; (2) the pre-occlusive phase in which angina occurs, often gradual before (3) the sudden onset of acute angina which differs from (2). The clinical recognition of a pre-occlusive state is admittedly difficult. The clinical history of acute angina is regarded as of more diagnostic value than the clinical signs. In 7.6 per cent of the cases of acute occlusion symptoms were absent; pericardial friction occurred in only 5 per cent.

Course and prognosis

Immediate mortality after acute coronary occlusion.—R. M. Woods and A. R. Barnes analyse 128 (males 108, females 20) cases of acute coronary occlusion, taken without special selection in order to investigate the factors influencing the immediate mortality rate after acute coronary occlusion within 6 weeks from the onset. Out of the 128 patients 68 survived and were living at the time this report was made; the remaining 60 patients died within 6 weeks from the onset. The immediate mortality rate for all patients under 50 years of age, of whom there were 32, was 28 per cent; for all between 50 and 59 it was 41.7 per cent; for those between 60 and 69 it was 57 per cent; and for those 70 years or more, 85 per cent. For all the above groups the immediate mortality was 47 per cent. The immediate mortality rate for males was 42 per cent, as compared with 75 per cent for women. Of the men 60 years of age or younger 34 per cent died within the period of 6 weeks as compared with 57 per cent of women in the same age group. The immediate mortality rate for men more than 60 years of age was 57 per cent as compared with 94.6 per cent for women in the same age group. The incidence of previous angina pectoris was 39.7 per cent among the patients who survived, and 40 per cent in the group of those who died within the period of 6 weeks. Of the 128 patients 62 gave electrocardiographic evidence of an anterior apical infarct, and 42 per cent of these 62 patients died within the immediate period; 52 patients had electrocardiographic evidence of a posterior basal infarct, and of these, 42 per cent died within the immediate period and the remaining 58 per cent survived. Eleven patients had an infarct which could not be localized on the electrocardiographic evidence, and of these 82 per cent died within the immediate period. Complications secondary to acute coronary occlusion influence the immediate prognosis to a great extent: pneumonia was present in 33 per cent of the deaths occurring within the immediate period; rapid and progressive enlargement of the liver was present in 15 per cent of the fatal cases and not in any survivals of the immediate period. Massive pulmonary embolism was the immediate cause of death in 10 per cent of all patients dying within the 6 weeks. The source of these clots was in the iliac vessels, not in the cardiac

cavities. Cerebral thrombosis occurred in 15 per cent of those who died, and in 2.9 per cent of those who survived the immediate period. Of the 17 patients who had very frequent ventricular extrasystoles after acute coronary obstruction 82 per cent succumbed during the immediate period. An electrocardiogram was in one case taken a few minutes before death from ventricular fibrillation. Pericarditis was recognized clinically in 10 per cent of the patients in whom death occurred within the immediate period, and in 1.5 per cent of the other cases.

Rehabilitation.—A. M. Master and S. Dack analysed the activities of 415 patients, 185 private and 234 in hospital, who had had an acute coronary occlusion and had survived the acute attack. In this series all types of occupation and all classes of society were represented. It was found that 53 per cent of all patients returned to work after recovery from the attack; this group of patients included 57 per cent of private patients, the remainder being ward patients. In 32 per cent of cases the work was full-time, and in 21 per cent part-time. In general the degree of economic restitution was greater in private than in the hospital patients. The factor of greatest importance in determining return to work was the age of the patient; 75 per cent of those in the fourth decade, but only 43 per cent of those in the seventh, resumed their occupation. Almost as many women (51 per cent) as men (54 per cent) returned to their former work. The percentage of patients returning to work after a first attack greatly exceeded that of patients who had had a second or third attack, being 59, 38, and 23 respectively. One man only resumed work after a fourth attack. Previous occupation was of some importance, 84 per cent of professional people, but only 50 to 55 per cent of other workers, resuming their occupation. Of 169 cases in which the time of return to work after getting out of bed was investigated, 92 per cent resumed work within one year, 76.5 per cent within 6 months, and 54 per cent within 3 months. Almost 56 per cent of patients who resumed work experienced some degree of pain, dyspnoea, or weakness while working. The chief cause of failure to return to work was physical debility due to angina pectoris, dyspnoea, or weakness.

Diagnosis

Quality of pain.—P. J. Steincrohn lays stress on the importance of recognizing the quality of the pain when diagnosing coronary thrombosis. The outstanding characteristic of the pain is its rhythm and periodicity. The patient must be observed carefully before the presence of the characteristics can be determined. The pain comes and goes in cycles. It is unbearable for a variable short period of time, and then subsides for a period equal to, or many times longer than, the actual pain. This cycle is usually repeated a number of times. To establish the presence of periodic pains the patient must be observed for at least 15 minutes to half an hour. If the periodicity of these pains is observed, the diagnosis of coronary thrombosis can be made.

Rupture of interventricular septum due to cardiac infarction.—R. H. Bayley and D. E. Fader record a case of rupture of the interventricular septum as a result of myocardial infarction in a man aged 47 years. This brings the number of recorded cases up to 23 and of those diagnosed correctly during life to 4. It is pointed out that the diagnosis should in most cases be quite simple. It depends on realizing that rupture is possible in a patient with clinical manifestations of cardiac infarction and the precordial signs of a septal defect; namely, a thrill and a loud systolic murmur over the centre of the praecordium; if the latter appeared after the onset of the infarction, the diagnosis is almost certain. At the necropsy in this event the basal region of the interventricular septum bulged moderately into the left ventricle and this formed part of the dilated infundibulum of the right ventricle. The apical third of the interventricular septum formed the right lateral wall of the aneurysmal sac at the apex of the left ventricle and protruded into the apical region of the right ventricle for a distance of 2.75 centimetres. At the apex of this protrusion there were three irregular openings which connected the two ventricles; the total area of these openings was approximately 2.5 square centimetres.

X-ray diagnosis of coronary artery disease.—G. Levene and R. M. Lowman state that X-ray diagnosis of coronary artery disease compares favourably with any other available method. The validity of the diagnostic criteria is strengthened by the ability to localize the area of involved myocardium. The accuracy of X-ray diagnosis of coronary artery disease as checked by necropsy in 38 cases was 89.5 per cent and the accuracy of electrocardiographic diagnosis 94.7 per cent. Of 33 cases localized at necropsy X-ray localization was fully in agreement in 72.7 per cent and the electrocardiographic diagnosis in 54.5 per cent.

Bayley, R. H., and Fader, D. E. (1941) *Amer. Heart J.*, **21**, 238.

Blumenthal, B., and Reisinger, J. A. (1940) *Amer. Heart J.*, **20**, 141.

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Levene, G., and Lowman, R. M. (1941) *Radiology*, **36**, 159.

Mackay, J. (1941) *Lancet*, **1**, 820.

Master, A. M., and Dack, S. (1940) *J. Amer. med. Ass.*, **115**, 828.

— and Jaffe, H. L. (1941) *Ann. intern. Med.*, **14**, 1155.

Nelson, M. G. (1940) *Ulster med. J.*, **9**, 94.

Steincrohn, P. J. (1940) *Ann. intern. Med.*, **14**, 495.

Woods, R. M., and Barnes, A. R. (1941) *Proc. Mayo Clin.*, **16**, 341.

ANIDROSIS

See also B.E.M.P., Vol. I, p. 584.

Congenital Ectodermal Defect*Clinical picture*

Familial incidence.—F. W. Sunderman reports 3 cases of hereditary ectodermal dysplasia of the anidrotic type occurring in three brothers. The salient features of the disease are the absence of sweat glands and occasionally of lachrymal glands, the growth of scanty, fine lanugo hair, the total absence of, or incomplete development of, the teeth, and the presence of chronic rhinitis, often associated with loss of the sense of smell. The chief complaints of these patients are fever and headache when exposed to high temperatures.

Sunderman refers to C. Darwin in 1896 as the previous recorder of so many subjects of hereditary ectodermal dysplasia of the anidrotic type in the same family. L. W. Lord and W. D. Wolfe collected more than 40 cases of absence of sweat glands. Two of Sunderman's patients were exposed for 30 minutes to a high temperature and compared with normal subjects: the loss of weight in these patients by evaporation from the lungs and skin corresponded approximately to that due to insensible loss at a normal temperature in the testing controls. The loss at the raised temperature shown by the controls was about 16 times that of the loss by the 2 patients, who became hyperpnoeic and showed increased output of urine. The controls were not affected by these symptoms.

Lord, L. W., and Wolfe, W. D. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 983.

Sunderman, F. W. (1941) *Arch. intern. Med.*, **67**, 846.

ANTHRAX

See also B.E.M.P., Vol. I, p. 629; Cumulative Supplement, Key No. 70; and Surveys and Abstracts 1940, p. 188.

Treatment*Serum and neokharsivan*

A. E. Hodgson reports 93 cases of cutaneous anthrax which were treated without surgical excision of the lesion by large doses of anthrax serum and neokharsivan given together intravenously. On the first day 100–250 cubic centimetres of serum and 0.3 milligram of neokharsivan are given. On the second the serum is repeated. On the third day the serum is repeated with 0.45 milligram of neokharsivan. On the fourth day serum is given, and on the fifth day serum plus 0.3 milligram of neokharsivan is administered. Of 52 patients to whom serum alone was given, 6 died, whereas in 41 who received serum and neokharsivan, all recovered.

Hodgson, A. E. (1941) *Lancet*, **1**, 811.

ANUS DISEASES

See also B.E.M.P., Vol. I, p. 643; Cumulative Supplement, Key No. 71; and Surveys and Abstracts 1939, p. 220; 1940, p. 189.

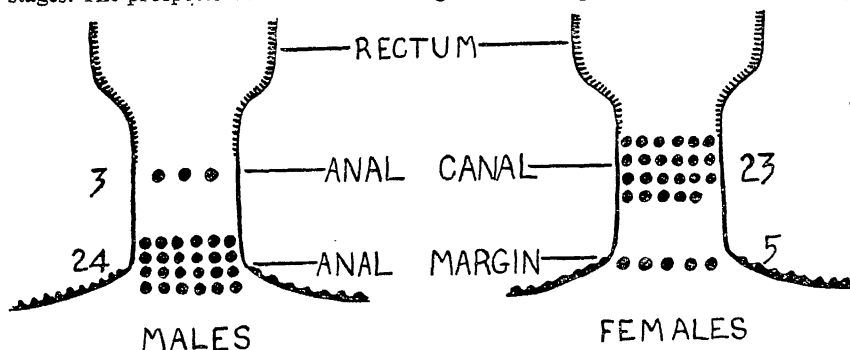
Pruritus Ani*Aetiology*

Faecal soiling of perianal skin.—E. Granet considers that, in many cases of pruritus ani, there appears to be a direct relation between faecal soiling of the perianal skin and the presence of pruritus. This is regarded as a dermatosis induced in the perianal skin by irritant substances in the faeces of specifically sensitive patients. The author found that a routine treatment directed to the prevention of faecal perianal soiling resulted in subjective and objective improvement in 93 per cent of 80 patients.

Carcinoma of the Anus*Clinical picture*

Squamous-celled carcinoma of the anus and anal canal.—W. B. Gabriel analyses 55 cases of primary squamous-celled carcinoma of the anus and anal canal admitted to St. Mark's Hospital, London, from 1922 to 1940, which occurred in 3.35 per cent of all cases of primary carcinoma of the rectum, anal canal, and anus admitted during that period. The sex incidence of the 55 cases was practically the same, but differed from that of primary adenocarcinoma of the rectum, which is nearly twice as common in males as in females. Primary squamous-celled carcinoma of the anal margin is chiefly a disease of men, whereas primary squamous-celled carcinoma of the anal canal is largely confined to women; the male liability to primary squamous-celled carcinoma of the anal margin may be related to the higher incidence in men of pruritus ani and of fistula in ano. To explain why women rather than men develop primary squamous-celled carcinoma of the anal canal it is suggested that chronic constipation and faecal impaction are more frequent in women and cause irritation, and that piles are also more common. The age incidence among the 55 cases averaged 61.7 years, which is higher than that of 57.4 which C. E. Dukes found to be the average age in 1,000 cases of adenocarcinoma of the rectum. The cases are divided into three grades of malignancy: (a) low grade—well differentiated, with much keratinization and numerous well marked cell nests; (b) medium grade—more cellular, with little differentiation, and few cell nests; (c) high grade—extremely cellular and undifferentiated, and usually with a total absence of keratinization. In one case only was a carcinoma in the anal region a basal-celled growth. Among the 55 cases there were 22 with low-grade malignancy, 10 being in an early stage and 8 of the 10

treated by radium treatment without colostomy and without inguinal gland dissection. In the medium-grade malignancy group there were 21 cases, 7 in early and 14 in late stages; and the 12 cases in the high-grade malignant group were equally divided as regards early and late stages. The prospects of cure in the low grade of malignancy by radium treatment or



excisionary surgery were found to be twice as high as those in the combined medium and high malignancy groups. Among cases treated by perineal excision there is likely, from the difficulty of closing the anus properly by suture, to be sepsis of the wound. The prophylactic use, both locally and orally, of sulphonamides is suggested.

R. W. Raven collected 19 cases (10 females, 9 males) between the ages of 34 and 78, average age 58 years, from the Royal Cancer Hospital, London, from 1929 to 1940. The patients were divided into those in stage (1), inguinal glands not palpable, 3; and those in stage (2), inguinal glands palpable, 16. The various methods of treatment employed are tabulated.

Gabriel, W. B. (1941) *Proc. R. Soc. Med.*, **34**, 139.

Granet, E. (1940) *New Engl. J. Med.*, **223**, 1015.

Raven, R. W. (1941) *Proc. R. Soc. Med.*, **34**, 157.

APPENDICITIS

See also B.E.M.P., Vol. I, p. 729; and Surveys and Abstracts 1939, p. 221; 1940, pp. 12 and 189.

Acute Appendicitis

Aetiology.

In old age.—In his account of acute appendicitis in the aged, H. Devine points out that, though it usually occurs in a crippled organ, atrophied, stenosed and dilated, fibrosed, disabled from a contained faecolite or arterially deficient from arteriosclerosis, it is often fulminating, perforating, or gangrenous, and that in half of the cases in patients over 60 shows perforation. In contrast to the disease in early life there is little reaction, the natural power of local defence being poor. The symptoms for the first few days are general, with perhaps mild, indefinite abdominal tenderness, but without nausea and vomiting; in more than half the cases the pulse and temperature are normal, and leucocytosis is rare. The diagnosis is therefore difficult, especially for those accustomed to the more stormy picture in young subjects. The course may be rapid, and many patients are moribund on admission to hospital. Operation is the only treatment of value, but the post-operative death rate may be as high as 30 to 35 per cent.

Treatment

Ambulatory.—D. J. Leithauser and H. L. Bergo recommend early ambulatory activity after operation. In 370 cases the patients, including those with chronic, mild, and acute appendicitis, and empyema and gangrene of the appendix, were subjected to the treatment. On the first post-operative day, after previous turning and deep breathing in bed, they sat on the edge of the bed, stood beside it for deep breathing, coughed to remove mucus accumulations, walked and returned to bed. The exercises were repeated under supervision. The average number of days of confinement to bed for the 370 cases was 1.5 and the average stay in hospital, 2.3 days after operation. The same methods were applied to 66 other surgical cases of various types. The average time of confinement to bed was 1.9 days. In the more serious cases, muscular contractions were performed in bed and the exercises out of bed proceeded more slowly. Improvement was generally rapid, many patients undertaking light work on the twenty-first post-operative day. The procedure is considered safe. There were not any cases of dehiscence, hernia, pneumonia, thrombophlebitis, or other serious complications (except one occurrence of fatal haemorrhage). The recumbent position appears to aggravate pulmonary and vascular complications by limiting thoracic treatment and by producing capillary dilatation and vasospasm. Early ambulatory activity should be avoided in cases of abdominal rigidity, abdominal or intestinal distension, insecure wounds, or severe shock.

Complications

J. F. P. Erasmus reports on the complications of acute appendicitis among 575 cases. Peritonitis occurred in 29.56 per cent, abscess in 13.22 per cent, subphrenic abscess in 0.17

per cent, pelvic abscess in 0·68 per cent, portal thrombophlebitis in 0·51 per cent, mechanical intestinal obstruction in 1·19 per cent, separation of ligatures on the stump of the appendix in 0·17 per cent, burst abdominal wall in 0·17 per cent, haematoma in 0·17 per cent, gross sepsis in 1·87 per cent, secondary haemorrhage in 0·17 per cent, faecal fistula in 1·02 per cent, bronchial complications in 1·53 per cent, femoral thrombosis in 0·51 per cent, and urinary tract infection in 0·68 per cent.

Post-operative acute hepatitis, jaundice, and abnormal bleeding.—F. A. Simeone and J. D. Stewart describe 2 cases illustrating the syndrome of acute hepatitis and hypoprothrombin-aemic bleeding after operation for acute appendicitis with perforation. Such bleeding may result in serious blood loss and extension of infection. Plasma prothrombin concentrations should be determined in cases of peritoneal infection of gastro-intestinal origin, and blood transfusions and parenteral vitamin K therapy should be given as indicated.

Oxyuris vermicularis.—W. V. Wax and N. S. Cooper found that in a series of 1,016 patients operated on for appendicitis, the incidence of *Oxyuris vermicularis* infestation was 0·007 per cent. The worm may be present in the appendix without causing symptoms of appendicitis. In children the worm produces a typical clinical picture of appendicitis, such as pain, vomiting, local tenderness, rigidity, and leucocytosis, and the reactions are more violent than those in adults. The oxyuris is rarely, if ever, found in suppurative and gangrenous forms of appendicitis.

Prognosis

Factors in lowered mortality rates.—L. Rumbold states that reports from various authors place the mortality rate from acute appendicitis at from 2·16 to 8·5 per cent. In the hospital to which Rumbold is attached the mortality rate has been steadily decreasing during the past 10 years until, in 1938, when there were 199 cases, it was only 0·5 per cent. The factors credited with the reduced mortality were (1) better post-operative care of the patient, (2) the use of the McBurney incision, (3) the closure of all wounds except in cases of well walled-off abscess.

Chronic Appendicitis

Clinical picture

J. H. L. Heintzelman and F. A. Evans from a clinical analysis of 300 hospital patients and 200 private patients with symptoms ascribed to disease of the vermiform appendix bring forward arguments against the belief that chronic appendicitis exists. Thus the symptoms may recur after appendicectomy; they may be psychogenic in origin, the old-fashioned nervous dyspepsia. Some cases are probably mild acute attacks of appendicitis. The authors suggest that it would be advisable to revert to the earlier conception, taught by pathologists, that true chronic appendicitis is very rare, if indeed it ever occurs. They have been unable to find an unqualified statement in any treatise on pathological anatomy by a recognized authority that any lesion can be properly called 'chronic appendicitis'.

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ARRHYTHMIA

See also B.E.M.P., Vol. II, p. 10; Surveys and Abstracts 1939, pp. 59 and 223; 1940, 191.

The Normal Cardiac Cycle

The electrocardiogram

Effects of fear.—F. Mainzer and M. Krause, while investigating the effect of an anaesthetic on cardiac action, made the observation that fear of an impending operation produced remarkable changes in the electrocardiogram of many persons with normal hearts. They therefore made a systematic examination of patients in the surgical and gynaecological departments of the Jewish Hospital, Alexandria. The following was the procedure as regards the taking of electrocardiograms: (1) one was taken on the day before an impending operation, of which the patient was then not aware, (2) the next was taken on the operation table, (3) another was taken while the patient was anaesthetized, and (4) one was taken a day or more after the operation. Of 53 patients (females 40, males 13) examined in this way, 12 showed an abnormal tracing on the day before operation (the rest electrocardiogram); 11 of these with coronary sclerosis, and one was undernourished qualitatively as well as quantitatively (avitaminosis) from carcinoma of the oesophagus. The 24 of the 53 patients who showed morbid tracings due to fear of an impending operation were divided into the following groups: (a) those with changes most often seen in coronary insufficiency, (b) those with changes usually seen in persons with neuro-circulatory asthenia or in connexion with hyperthyroidism, (c) those with the changes described under (a) and (b). These changes due to fear occur in the young as well as at higher ages. In most of the cases showing this fear-reaction there is a return to the normal a day after the operation. Death from cardiac failure on the operating

table immediately before the induction of general anaesthesia, as well as during anaesthesia, should in some cases at least be regarded as the extreme outcome of an otherwise usual fear-reaction.

Tachycardia

Paroxysmal tachycardia

Symptoms.—J. P. Hubbard reviews 9 cases of paroxysmal tachycardia in young infants. The clinical picture in such cases is distinctive. The heart rate is generally 250 to 300, and if this continues for several days, as it is likely to do, it leads to circulatory failure, associated with vomiting, dyspnoea, fever, leucocytosis, cardiac enlargement, pulmonary congestion, and engorgement of the liver. The disease responds satisfactorily to adequate doses of digitalis.

Bundle-branch Block

Relation to cardiac enlargement

A. M. Master, H. Kalter, S. Dack, and H. L. Jaffe studied the size of the heart at necropsy or by X-rays in 100 cases of bundle-branch block. The heart was enlarged in all cases examined after death, the average weight being 586 grammes and the lowest 375 grammes. Of the cases examined radiologically, the heart was enlarged in 91 per cent. In 3 of the 6 cases without enlargement, the diagnosis was toxic goitre. Left bundle-branch block was present in 90 per cent of the cases; in 71 per cent of these the left ventricle was larger than the right. Hypertensive heart disease was present in almost all cases of left bundle-branch block. Of the 10 cases of right bundle-branch block, the right ventricle was predominant in 4 and the left in 1. Diffuse myocardial involvement was found in all cases at necropsy. It is concluded that, in most cases, chronic bundle-branch block results from an increase in size of the heart, myocardial damage, and diffuse involvement of the bundle-branch system.

Auricular Flutter and Auricular Fibrillation

Auricular fibrillation

Aetiology.—I. C. Brill and W. A. Meissner, as a result of examination of the records of the necropsies of 400 cases of auricular fibrillation, found that in the absence of congestive heart failure or acute coronary occlusion, coronary artery disease is not a cause of auricular fibrillation. Congestive heart failure involving the left side of the heart tends to favour the development of auricular fibrillation. The authors suggest that stretching of the left auricle may be an important factor in this process. Coronary artery disease may, however, be an indirect factor in the causation of auricular fibrillation by first inducing congestive heart failure.

Ventricular Fibrillation

Mechanism

C. J. Wiggers, explaining the mechanism of ventricular fibrillation, states that, in order to initiate fibrillation, an electrical stimulus or noxious influences with a 'fibrillation threshold' must be applied during the vulnerable period of late systole, when certain elements have passed out of the refractory phase. Such a stimulus excites impulses in a number of non-refractory fractions. These weave their way slowly through local non-refractory tissue to form a small wave front, from which a massive excitation wave sweeps over comparatively large portions of the myocardium in sequential order. This constitutes the first premature systole. If the wave front is large enough, and the mode of spread favourable for re-entry at, or near, the point of excitation, several circuits are formed through the ventricles; this is the undulatory stage. In some way these masses of myocardium are broken into smaller and smaller ones, in which divided waves re-enter more frequently. Thus the process passes successively into the convulsive and tremulous stages; during the latter there are innumerable avenues of re-entry. The atonic stage is characterized by progressive enfeeblement of contraction and gradual failure of conduction, which are the result of anoxia caused by cessation of the coronary circulation.

Extrasystoles

Treatment

Potassium chloride.—L. I. M. Castleden reports that the administration of potassium salts caused the disappearance of extrasystoles in one case in which they were associated with insulin hypoglycaemia, and in 4 spontaneous cases. In 3 of these cases in which the level of serum potassium was estimated, the disappearance of extrasystoles was associated with a rise in potassium level. A dose of 6 grammes of potassium chloride, by mouth, generally caused disappearance of the extrasystoles in half an hour to an hour.

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ARTERIAL DISEASE AND DEGENERATION

See also B.E.M.P., Vol. II, p. 39; Cumulative Supplement, Key Nos. 86-93; Surveys and Abstracts 1939, pp. 61 and 224; 1940, p. 193; and p. 2 of this volume.

Mechanism of the Arterial Circulation

Action of vasodilator drugs

Plethysmographic method of measuring peripheral flow.—D. I. Abramson, H. Zazella, and N. Schkloven investigated the vasodilator action of therapeutic agents commonly used in the treatment of peripheral vascular diseases. The rate of peripheral flow was measured in 31 patients with peripheral circulatory impairment, by the plethysmographic method. Readings were taken at 10-minute intervals after a single administration. Calcium gluconate, padutin, papaverine, spasmalgin, and thiamine chloride did not increase, or only very slightly, the flow to the hand, forearm, leg, and foot. Alcohol, stilboestrol, and histamine increased the flow to the hand in most cases. Prostigmin was effective in half, and hypertonic salt solution in one-third of the tests. Venous occlusion pressure applied intermittently for 2 or 3 hours did not produce a significant increase in flow. The different results produced by the method of the skin thermometer and oscilometer indicate that temperature is not necessarily a criterion of vasodilatation. B. Jablons in a discussion criticized the plethysmographic technique on the grounds that stasis in venous capillaries resulting from certain drugs, such as nicotinic acid, increased the volume of fluid in the extremities and gave a false impression of increased flow. Moreover, the temperature technique included muscular temperature, amplitude of peripheral pulsations, and microscopic capillary examination. N. D. Wilensky pointed out a certain artifact in the plethysmographic technique. In reply D. I. Abramson pointed out that when proximal venous occlusion pressure was applied, any swelling of the extremities depended on the rate of inflow of the blood. The quantity of blood flowing in during the first second of occlusion could also be measured. The presence of the artifact was denied.

Method of increasing the arterial flow to an extremity

By venous occlusion.—A. L. Libby demonstrated experimentally the therapeutic value of venous occlusion in increasing the arterial flow to an extremity. A thermostromuhr was used on anaesthetized dogs and enabled accurate measurements of the minute volume of blood flow to be taken. Occlusion was found to increase the arterial blood flow to the extremity. The increase was localized and probably not of humoral or nervous origin. A less rapid increase was induced in a deficient arterial flow, suggesting that intermittent venous pressure can be used in chronic obliterative vascular disease. The rate of increase was found to vary directly with the degree of venous pressure. Gradually increasing pressure applied with a tourniquet was followed by an exactly corresponding increase of arterial flow up to the level of systolic pressure. The use of the tourniquet was found to be more effective than the ligation of the main vein. It is suggested that the increase in arterial flow may be due to venous enlargement and accompanying capillary enlargement, hence, in occlusion therapy, the congestive period should be longer than the less important release period.

Periarteritis Nodosa

Clinical picture

J. Lebowich and H. D. Hunt report a case of periarteritis nodosa in a man aged 56. The clinical picture of this disease is protean and may simulate any condition including sepsis and infection. Eosinophilia, especially with a leucocytosis in the presence of a rather bizarre symptomatology that does not seem to fit any syndrome, should strongly suggest periarteritis nodosa.

Thrombo-Angiitis Obliterans (Buerger's Disease)

Aetiology

Tobacco.—F. V. Theis and M. R. Freeland report on investigation on the result of smoking in the aetiology of thrombo-angiitis obliterans. They find that tobacco smoking was generally accompanied by a greater reduction in the oxygenation of the arterial blood in patients with this disease than in ordinary individuals. The extent of the reduction seemed to be influenced by physiological adjustments in the blood pressure, pulse rate, and peripheral skin temperatures.

Chronic Arteritis

Definition and classification

'Ageing' of arteries.—S. W. Sappington and J. A. Horneff follow up the report on the radial artery in comparison with the state of the coronary and other arteries in 86 cases by Sappington and H. S. Cook, by the present research on the changes in the tibial artery in comparison with those in the radial and coronary arteries of 61 cases, in order to contrast the differences at various age periods. The age distribution of the 61 cases was as follows: up to the age of 40, 11 cases, in the fifth decade 13, in the sixth 14, in the seventh 14, and in the eighth and after, 9 cases. There were 35 males and 26 females. The 61 cases covered a number of diseases, the only ones purposely avoided being those presenting definite evidence of arterial obstruction in the extremities; thus cases of arteriosclerosis and thrombo-angiitis obliterans were excluded. In each case sections were taken from the lower anterior tibial artery just before it passes into the dorsalis pedis artery, from the radial artery at the wrist, and from the right and left circumflex and anterior descending branches of the coronary arteries. The appearances of these arteries in each case were compared. Except in connexion with the occurrence of gangrene, the changes in the tibial arteries, confirmed by routine histological examination as in this series, are few as compared with those of the radial artery. In the large coronary arteries the changes accompanying advancing years reach a high degree of incidence; as

might be expected, the changes in the tibial artery are comparable with those in the radial rather than with those in the coronary arteries. The incidence of arteriosclerosis is slightly higher in the tibials than in the radials, especially after the age of 60. The well-known greater liability of the arteries of the lower extremities to calcification of the middle coat was confirmed: thus it was present in 47.5 per cent of the 61 tibials, but in only 14.7 per cent of the 61 radials; under the age of 50 years it was found in 7 out of 24 tibials, but in none of the radial arteries. Altogether the intimal thickening in the tibials, as well as in the radials, is slight, especially as compared with that of the coronaries, and seldom threatens the integrity of the lumen. As in the case of the radial, the anatomical state of the tibial artery has not any inferential bearing on coronary sclerosis.

Aetiology

Tobacco smoking and coronary disease.—J. P. English, F. A. Willius, and J. Berkson examined 1,000 records of established coronary disease in a clinic with a view to discovering the effect of tobacco smoking on the condition. It appears from this that there is a higher incidence of coronary disease among smokers than among non-smokers in the fifth decade, and perhaps that of 50 to 59. The incidence of the disease in those under 50 was greatest among excessive smokers, least among non-smokers, and occupied an intermediary position among moderate smokers. This was not true in those above 59.

Pathology: arteriosclerosis and arteriolosclerosis

Infantile arteriosclerosis.—A. H. Baggenstoss and H. M. Keith describe the case of an infant, aged 8 weeks, dying in a much dehydrated state after vomiting. At the necropsy the only gross abnormality was the heart, which weighed 43 grammes as compared with the normal (23 grammes) for that age. The coronary arteries were tortuous, sclerotic, and practically occluded. The left ventricle was dilated and there was chronic infarction of the myocardium. Microscopically the inner part of the muscular media of the coronary arteries showed numerous deposits of calcium, sometimes forming a complete ring; near these deposits there was in the intima fibroplastic proliferation with numerous giant cells causing arterial narrowing. Similar changes were present in the small arteries of the mesentery, kidneys, and peri-adrenal tissue, and in the aorta and pulmonary artery. The kidneys showed arteriolar sclerosis. The cause of the calcification is discussed, and it is possible that there was an abnormality of the arterial wall as a result of either infection or incomplete development, or a severe disturbance in calcium metabolism, such as might be due to overdose with vitamin D; a combination of these two mechanisms might have been responsible. The first recorded case was probably that by Durante in 1901; the authors have collected 8 other similar cases. In 5 of the 9 cases the presence of calcium was found in the organs as distinct from their blood vessels; this would reasonably suggest hyperparathyroidism. In recording this case of the rare condition of arterial calcification in infancy, Baggenstoss and Keith discuss the possibility that it may be the result of healed periarteritis nodosa, but conclude that this interpretation is hardly tenable, as calcification has not been observed in periarteritis nodosa.

Clinical picture

Thrombosis of temporal artery.—J. M. Bowers reports a case of inflammation selectively involving the temporal arteries and differing pathologically and clinically from thrombo-angiitis obliterans, periarteritis nodosa, and rheumatic arteritis. The patient was a woman, aged 65, with hypertension and severe headache; both temporal arteries, but particularly the left, were thickened, tortuous but not nodular; the occipital arteries were similarly affected. Biopsy of a branch of the left temporal artery showed an organized thrombus, thinning of the intima, infiltration of the media with mononuclear cells, polymorphonuclear and eosinophil cells, and granulation tissue. Cultures from the artery showed Gram-positive cocci. There was relief of pain after the removal of a segment of an affected artery. This is stated to be the sixteenth case put on record. A review of these cases shows that both sexes are affected; the patients are usually more than 60 years of age and often hypertensive and arteriosclerotic. The illness lasts for about 6 months, and, although relapses may occur, it tends to subside completely, thus differing from periarteritis nodosa which usually proves fatal within a year. Microscopically the morbid changes are centred on the middle coat, which shows moderate necrosis, sometimes haemorrhages; granulation tissue with numerous giant cells form in the destroyed areas.

P. H. Sprague and W. C. MacKenzie record the thirteenth recognized example of the condition of temporal arteritis of which Horton and Magath (1937) collected 9 cases. A man, aged 66, complained of pain in the left side of the face, at first regarded as atypical temporal neuralgia; a week later more severe pain occurred on the right side of the face, about the temporo-mandibular joint, and later the temporal arteries became inflamed, hard, and tender, biopsy showing obliterative arteritis, the muscular media being fibrotic, and all the coats showing extensive lymphocytic infiltration with, in some areas, giant cells of the foreign body type. The patient showed some evidence of septic foci, became anaemic, lost appetite and weight, and became mentally dull. Eventually, however, improvement set in. Horton and Magath suggested that the headache was due to involvement of the cerebral arteries. Differential diagnosis must be made from periarteritis nodosa, thrombo-angiitis obliterans, and rheumatic arteritis. It is stated that the condition is probably not very rare.

Intercapillary glomerulo-sclerosis and diabetes mellitus.—W. B. Porter and H. Walker state that intercapillary glomerulo-sclerosis is an accelerated ageing process occurring in mild

diabetes mellitus, and that it is accompanied by wide-spread arteriosclerosis. The well-developed syndrome is characterized by mild diabetes mellitus, albuminuria, varying degrees of hypertension, arteriosclerosis, oedema, and hypoproteinaemia. The development of the renal changes alters the clinical course of an otherwise mild diabetes mellitus to a serious and progressive malady.

Occlusion of the abdominal aorta.—The classical clinical picture associated with complete occlusion of the aorta at its bifurcation is that of acute onset with severe pain and loss of sensation in the legs, absence of arterial pulsation, rapidly progressive gangrene of the legs, and almost always a fatal outcome. In 7 cases, in which complete obstruction of the aorta was found at necropsy, H. Gross and B. Philips found this typical clinical course in one only. In 4 cases atherosclerosis involved the aorta and coronary arteries. In this group 1 patient presented the classical symptoms; in another there was nothing in the clinical course to suggest occlusion of the aorta. In the other 2 gangrene progressed rapidly. In 2 cases diffuse vascular disease was present, arterial in one and venous in another. The seventh was a case of chronic rheumatic cardiovascular disease with arrhythmia and intracardiac thrombi. The authors attribute the variations in the clinical picture to differences in the rate of development of occlusion and of formation of a collateral circulation.

Diagnosis

Coeliac axis calcification and X-ray appearance.—According to W. W. Fray, calcification of the arterial walls of the coeliac axis is frequent in elderly subjects. The location of the shadows is typically over the left upper quadrant, the proximal branches lying at the level of the dorsi-lumbar junction, the more distal branches varying widely and shifting in position with the organ supplied.

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ARTHRITIS: OSTEOARTHRITIS

See also B.E.M.P., Vol. II, p. 91; Cumulative Supplement, Key No. 100; and Surveys and Abstracts 1939, p. 228; 1940, p. 200.

Treatment

Surgical

F. D. Dickson states that in cases of arthritis which have reached the quiescent stage surgery is useful in the correction of disabling joint deformities, relieving pain, and improvement of function. The number of persons apparently incapacitated by chronic arthritis whose condition may be benefited by surgery is considerable. The procedures most generally employed are manipulation, in which the capsule and ligaments are the chief cause of the deformity; capsuloplasty, in which the capsule and ligaments are widely involved; synovectomy, for removal of infection and when the synovia and cartilages are much involved; arthroplasty, to restore motion in ankylosed but important joints and arthrodesis, when stability is more important than movement.

Dickson, F. D. (1941) *Ann. Surg.*, **113**, 869.

ARTHRITIS: RHEUMATOID ARTHRITIS

See also B.E.M.P., Vol. II, p. 74; Cumulative Supplement, Key No. 98; and Surveys and Abstracts 1939, p. 226; 1940, p. 198.

Aetiology

Vitamin A deficiency

M. G. Hall, T. B. Bayles, and P. Soutter found that patients with rheumatoid arthritis showed much higher average dark-adaptation curves than a group of controls, as measured by the biophotometer. Of 79 patients with rheumatoid arthritis, 65 per cent showed abnormal dark-adaptation curves. These high readings may be interpreted as an indication of borderline to severe vitamin A deficiency. Supplemental doses of from 25,500 to 68,000 U.S.P. (United States Pharmacopoeia) units of vitamin A per day were necessary to establish and maintain

normal levels. In 45 cases tested the degree of vitamin A deficiency was roughly parallel with the severity of the disease, as indicated by the erythrocytic sedimentation test. In patients receiving adequate vitamin A therapy, no obvious clinical improvement was seen which could be ascribed to the effect of the vitamin.

Diagnosis

Formol-gel reaction

According to C. W. Scull and R. Pemberton the formol-gel reaction in the blood plasma and serum of patients with rheumatic diseases is reasonably suitable as an index of the extent of systemic activity of the morbid process. Although less exact as a quantitative measurement than certain other measures, the test is sufficiently simple and sensitive to be employed as a routine procedure. Patients with active atrophic (rheumatoid) arthritis or mixed arthritis generally give positive reactions, whereas those with hypertrophic (osteoarthritic) arthritis show less definite positive reactions.

Pathology

Cardiac lesions

A. H. Baggenstoss and E. F. Rosenberg review the present opinion about the presence and nature of cardiac lesions associated with chronic infective (rheumatoid) arthritis, and contribute a post-mortem study of 25 cases of this disease from the records of the Mayo Clinic where the diagnosis during life had been made by a consultant of the Section on Arthritis. Cardiac lesions were found in 20 cases, in only two of which was a history of rheumatic fever forthcoming. Lesions identical with those of rheumatic fever were observed in 14, or 56 per cent; as the myocardium showed rheumatic lesions in 12, the mitral valve alone was involved in 6, the mitral and aortic valves in 3 more. Non-rheumatic cardiac lesions were present in 6 (24 per cent). In 10 of 14 cases in which there were rheumatic lesions, there was histological evidence that the inflammatory process was still active and progressive at the time of death. In 7 of 14 cases associated with rheumatic cardiac lesions, the heart disease was regarded as an important factor in causing death. In only 7 of the 14 cases with rheumatic heart lesions had signs or symptoms of rheumatic cardiac lesions been present during life.

Extra-articular lesions

A. H. Baggenstoss studied 25 cases of chronic infective (rheumatoid) arthritis for extra-articular lesions. Necropsy revealed cardiac lesions in 20 of the 25 cases. In 14 cases (56 per cent) the lesions were indistinguishable from those of rheumatic fever. In 6 cases, or 24 per cent, the cardiac lesions were non-rheumatic. In 10 of the 14 cases in which rheumatic lesions were demonstrated, there were histological appearances to suggest that the inflammatory process had still been active and progressive at the time that death occurred.

Treatment

Gold salts

P. Ellman, J. S. Lawrence, and G. P. Thorold divided 90 typical cases of rheumatoid arthritis into three equal groups. Two groups of patients were treated with large and small doses of solganal B (aurothioglucose) respectively, and one group was used as a control. The dosage in one group was 0.2 gramme weekly, sometimes increased to 0.3 gramme. The other group was given 0.1 gramme weekly. Injections were given intramuscularly. The period of treatment was 9 months. Aurothioglucose can alter favourably the course of the disease. Of the patients treated by the larger dose method, in 14 (47 per cent) the disease was rendered inactive; of the patients treated by the small dose method, in 8 (27 per cent) the disease became inactive; and of the controls, in 1 (3 per cent) the disease became inactive. Toxic effects have attracted attention from several workers. Of 25 cases of gold intoxication collected by Ellman, Lawrence, and Thorold nearly all have been in the presence of a normal sedimentation rate. It is remarkable how often dermatitis and stomatitis appear if the gold injections are continued after the sedimentation test has become normal. The most important of the toxic effects are stomatitis, exfoliative dermatitis, toxic jaundice, aplastic anaemia, agranulocytosis, and purpura.

In a review of present tendencies in arthritis, R. L. Cecil points out that the hypothesis of focal infection as responsible for rheumatoid arthritis is very much on the wane and indeed urgently needs complete reevaluation. A more conservative attitude should be adopted as regards infected tonsils, sinuses, and teeth. There is a form of infective arthritis, not rheumatoid, which is related to focal infection and is benefited by removal of infective foci. The treatment of rheumatoid arthritis by gold preparations has been carried out by Cecil in more than 200 patients with increasing success, especially with myocrisin (sodium aurothiomalate). It may, however, be dangerous; though Cecil has not seen any serious blood changes he reports 3 cases of exfoliative dermatitis, 2 of them quite severe. Fever therapy has been extensively tried, and the results are fairly consistent; most of the patients are temporarily benefited but relapse later. The effect of jaundice on rheumatoid arthritis, whether the jaundice is natural or specially induced, seems to be a temporary palliative not a cure.

Splints and physiotherapy

J. Bastow recommends local treatment (1) to prevent deformity, (2) to correct an established deformity, and (3) to prevent insidious recurrence of deformity during remissions of the disease. (1) The onset of deformity in arthritis deformans is extremely insidious, consisting

at first of slight flexion in a joint coming on at night, and later slow loss of extension. The application of a perfectly fitting splint during the acute stage relieves pain, spasm, and the production of deformity; but as there is great liability to the formation of extra- and intra-articular adhesions if the joint is absolutely immobilized, this should be obviated by daily removal of the plaster splint so as to allow treatment by gentle movements and physiotherapy. Only by the combined use of local splintage and physiotherapy can good results be obtained. At the Royal National Hospital for Rheumatism, Bath, a technique for the application of thin, light, skin-tight, carefully moulded plaster of Paris splints has been worked out. They are applied by means of a plaster slab and encircling bandage, either directly to the skin or over one layer of stockinette. After 24 or 48 hours these splints are slit down each side and then used as anterior and posterior shells, being fixed to the limbs by straps and buckles. As the acute symptoms subside, the patient is allowed short but gradually increasing periods of exercise out of splints, which are always worn during rest and at night. When the patient leaves the hospital the splints are taken home and used as night splints. (2) In acute cases with early established deformity, skin-tight plasters are applied in the position of deformity, no attempt being made to force the limb into the corrected position. After 24 to 48 hours the plasters are bivalved and physiotherapy begun; by massage and re-education the muscles opposing the position of deformity should be built up. (3) For the prevention of recurrence of deformity three points are emphasized: (a) rest plasters should be worn regularly at night for several months after discharge, and at once resumed on any sign of renewed activity; (b) active non-weight-bearing exercises must be continued; (c) the bodily posture as a whole should receive attention so as to eliminate faulty position and allow the starting of corrective exercises.

Bee venom

J. L. Hollander reports on the treatment of 42 patients with rheumatoid arthritis and osteoarthritis by two brands, ven-apis and lyovac, of bee venom given hypodermically over the extensor surfaces of the most painful joints; ven-apis was given to the first 22 patients, and lyovac bee venom to the remaining 20. Three patients were markedly improved, 5 more moderately improved, and 9 experienced some relief during the course of treatment, but relapsed when the injections were discontinued. Twenty-two patients were not influenced, and 3 were worse after the treatment. Most of the patients were injected 20 times or more, the equivalent of 100 or more bee stings, and none less than on 6 occasions. Each of the 17 controls was given 15 injections, intravenously or intramuscularly at weekly intervals, of proteolac, a milk protein solution; 3 of these controls were perceptibly improved, 5 more were better only while receiving the treatment, and the remaining 9 were not affected; no untoward results were seen. In a footnote the editors point out that the word 'controls' must be used with reservation because proteolac might cause a non-specific protein shock. Bee venom is described as an albumin-free sapotoxin allied to snake venom combined with a poison resembling cantharides; it contains some histamine but not any formic acid. Other forms of bee venom for injection available for accuracy of dosage and avoidance of direct bee stings are apicosan and apicur.

Baggenstoss, A. H. (1941) *Proc. Mayo Clin.*, **16**, 232.

— and Rosenberg, E. F. (1941) *Arch. intern. Med.*, **67**, 241.

Bastow, J. (1940) *J. chart. Soc. Massage med. Gymn.*, **26**, 132.

Cecil, R. L. (1940) *Proc. Mayo Clin.*, **15**, 556.

Ellman, P., Lawrence, J. S., and Thorold, G. P. (1940) *Brit. med. J.*, **2**, 314.

Hall, M. G., Bayles, T. B., and Soutter, P. (1940) *New Engl. J. Med.*, **223**, 92.

Hollander, J. L. (1941) *Amer. J. med. Sci.*, **201**, 796.

Scull, C. W., and Pemberton, R. (1941) *Ann. intern. Med.*, **14**, 993.

ARTHRITIS: SPONDYLITIS

See also B.E.M.P., Vol. II, p. 105; and Surveys and Abstracts 1940, p. 200.

Ankylosing Spondylitis

Spondylarthritis ankylopoietica

C. L. Dunham and F. G. Kautz record notes of 20 patients, all males, with a form of chronic spondylarthritis, among 2,395 patients registered at the Desert Sanatorium, Tucson, Arizona. This condition is distinct from spondylitis deformans, but whether it is a disease *sui generis* or the spinal form of atrophic (rheumatoid) arthritis is difficult to decide; in fact its causation is as debatable as is that of rheumatoid arthritis. It is a chronic, progressive, probably infective, disease of the spinal column and adjacent structures, chiefly in young males, and characterized clinically by pain and stiffness in the back with or without involvement of the hip and shoulder joints. There is early ankylosis of small posterior intervertebral articulations and of the sacro-iliac joints, and atrophy of the vertebral bodies which do not collapse. The costochondral joints may become ankylosed, and calcification of the longitudinal ligaments of the spine may produce the so-called bamboo spine. Exacerbations and remissions may progress in the absence of pain. Twenty tabulated cases are analysed and compared with the observations of others. The question of an infective origin is considered; in 14 cases there was consistent evidence of a low-grade infection of the urinary tract. In 5 cases there was evidence of tuberculosis, but the authors do not consider this to be a causal factor; it must be remembered that a considerable number of tuberculous patients are attracted to the Desert Sanatorium.

Iritis has not often been noticed in the disease; it occurred at one time or another in 5 of the 20 cases; but in none of the patients with active or inactive tuberculosis was there iritis.

Dunham, C. L., and Kautz, F. G. (1941) *Amer. J. med. Sci.*, **201**, 232.

ASCARIASIS

See also B.E.M.P., Vol. II, p. 146; Cumulative Supplement, Key No. 105; and Surveys and Abstracts 1939, p. 230.

Treatment

Phenothiazine

According to P. Manson-Bahr phenothiazine (thiodiphenyl-amine) is an effective anthelmintic in roundworm and threadworm infections. Nine patients with *Ascaris lumbricoides*, 5 with a double infection with roundworms and hookworms and 2 with a double infection with roundworms and whipworms, were treated. The total dosage ranged from 16 to 48 grammes. Only one roundworm recovered and the whipworms were unaffected. In 2 other patients with multiple infections who were given 8 grammes of the drug daily for 3 days, followed by a dose of sodium sulphate, all the roundworms were removed. The drug gave good and permanent results in threadworm infections, especially in children. Of 6 children and 3 adults treated, all were cured. The dosage recommended is as follows: for children under 8, 2 grammes daily for 7 days; for children under 4, 1 gramme daily for 7 days; and for adults, 8 grammes daily for at least 5 days.

Manson-Bahr, P. (1940) *Lancet*, **2**, 808.

ASPHYXIA IN CHILDREN

See also B.E.M.P., Vol. II, p. 173; Cumulative Supplement, Key No. 109; and Surveys and Abstracts 1939, p. 231.

Asphyxia during the Early Weeks of Life

Causes

General review.—H. Henderson, E. B. Foster, and L. S. Eno analyse the records of 975 consecutive unselected deliveries by one operator from the point of view of factors which might produce asphyxia in the new-born. A slight preponderance of deliveries under general anaesthesia was noted. Of the 975 infants, 90.6 per cent did not need resuscitation. Of those requiring resuscitation, 5.2 per cent were revived simply by aspiration of the trachea and the administration of oxygen and 5 per cent carbon dioxide; 1.3 per cent required artificial respiration, and 1.9 per cent were still-born. None of the 18 still-births could be attributed to the means of delivery, or to the use of either analgesics or anaesthetics. A total of 95.4 per cent of those in the local anaesthesia group, and 88.3 per cent of those in the general anaesthesia group breathed spontaneously. Severe asphyxia occurred in the same percentage in the entire series, namely, 1.3 per cent.

Treatment

J. D. Russ and R. A. Strong describe a method of dealing with asphyxiated infants. After the cord is cut, the baby is received by the paediatrician in a sterile towel, and placed on the table. It is wrapped in a warm cover, and the skin is gently rubbed for a few seconds, and the head is then hyperextended. With the intratracheal catheter, the nostrils, mouth, pharynx, and nasopharynx are immediately aspirated for mucus and other fluids. If respiration does not begin, plain oxygen by the face-mask is given for several minutes, until the respirations are regular in volume and rate, or until the baby cries. If respiration does not begin, alpha-lobeline is given by way of the umbilical vein, and the intratracheal catheter is introduced into the trachea, and any fluid aspirated. From 5 to 10 gentle inspirations and expirations are made through the catheter. If respiration has begun, oxygen is again given by the face-mask. Coramine in doses of 2 minims (0.12 cubic centimetre) is given subcutaneously if the beat of the heart flags. When respiration is established, all moderately or severely asphyxiated infants are placed in an incubator, or kept warm under an oxygen tent for at least 12 hours.

Helium-oxygen mixture.—H. F. Kane employed a mixture of 80 per cent of helium and 20 per cent of oxygen in 200 newly-born babies, few of whom were deeply asphyxiated, and some not at all. Immediately after the cord was cut the baby was placed in a respirator and the gas mixture administered. In all the cases of light asphyxia, the infants responded more quickly to the mixture than to pure oxygen. In several cases of deep asphyxia, after oxygen had been used without success, the addition of helium was followed by almost immediate clearing of cyanosis and prompt respiratory movements.

Oxygen therapy.—N. J. Eastman states that, in the presence of anoxia, apnoea neonatorum is resistant to all types of treatment other than correction of the anoxia. The only method of initiating respiration in such cases is by the administration of oxygen. Treatment consists in the application of warmth, keeping the head declined about 30 degrees to favour gravity drainage of fluids in the trachea, aspiration of mucus by means of a catheter, and insufflation of 100 per cent oxygen.

Eastman, N. J. (1940) *Amer. J. Obstet. Gynec.*, **40**, 647.

Henderson, H., Foster, E. B., and Eno, L. S. (1941) *Amer. J. Obstet. Gynec.*, **41**, 596.

Kane, H. F. (1940) *Amer. J. Obstet. Gynec.*, **40**, 140.

Russ, J. D., and Strong, R. A. (1941) *Amer. J. Dis. Child.*, **61**, 1.

ASTHMA

See also B.E.M.P., Vol. II, p. 179; Cumulative Supplement, Key No. 110; and Surveys and Abstracts 1939, p. 231; 1940, p. 202.

Aetiology*Relation to ascorbic acid*

Increase of demand for vitamin C.—Grace A. Goldsmith, A. T. Ogaard, and D. F. Gowe state that, though many divergent views have been expressed, there appears to be some relation between the amount of ascorbic acid in the blood and the incidence and severity of asthmatic attacks. Thirty-two patients were investigated, 9 for 11 to 35 weeks; 29 had bronchial asthma, and of these 17 had hay fever and 4 urticaria as additional allergic manifestations. The amount of ascorbic acid in the fasting blood was found to be subnormal in 19 patients and in only 3 out of the 32 patients was the level in the blood above 1.0 milligram which would be generally accepted as evidence of excellent vitamin C nutrition. The data obtained indicate that in asthma there may be an increased demand for a supply of vitamin C; it is suggested that exertion such as that in an asthmatic attack may be connected with this requirement for more vitamin C. In 2 patients, when the blood was saturated with ascorbic acid the condition of these persons was much improved. In 5 other patients, however, the asthma was not appreciably influenced by the administration of ascorbic acid.

Exposure to gum acacia

C. B. Bohner, J. M. Sheldon, and J. W. Trenis report 10 cases of printers in whom direct exposure to gum acacia provoked severe asthmatic attacks. Exposure was due to sprays used in the printing industry. The interval between the first exposure and the onset of asthmatic symptoms varied from 2 weeks to 12 months. Eight of the patients were adult males, their ages ranging from 22 to 53. The increasing use of gum acacia in the printing of magazines and in box labelling suggests the possibility of more wide-spread allergy to acacia. The authors suggest that dextrose be substituted for acacia in offset sprays.

Specific sensitization

Relation to infections of upper respiratory tract.—W. H. Turnley, as a result of a questionnaire sent to 300 practitioners on the relation of bronchial asthma to infections of the upper respiratory tract, made the following observations: 91 per cent of the replies showed that sinusitis is the chief focus and that the asthmatic patient may be benefited by treatment of the sinusitis; 35 per cent of the replies stated that treatment of a chronically discharging ear may relieve asthma; 40 per cent that dental sepsis may be a source of infection influencing asthma; 60 per cent that infection of the tonsils was a causal factor, and 80 per cent infection of the adenoids; 40 per cent that asthma may be prevented in later life by the removal of infective foci from children as soon as the asthma is noted. With regard to the endocrine organs, 67 per cent of the replies held that these glands were an effective causal factor. Other factors said to influence asthma were infection (92 per cent), season (82 per cent), fatigue (82 per cent), and emotional instability (70 per cent).

Clinical Picture*Types in adults*

Pulmonary eosinophilia.—R. Freund and S. Samuelson record a case in a woman, aged 25, of transitory infiltration of the lung with eosinophils (Löfller's syndrome), and bring the reported cases up to 105, of which W. Löfller (1936) recorded 51. The four cardinal signs are: indications of pulmonary disease on auscultation and percussion, the presence of a corresponding shadow radiologically, temporary character of the pulmonary signs, and increase of the eosinophils in the blood. The symptoms are so mild that the patients rarely consult a medical practitioner; but the physical signs, which in the case reported lasted about a week, are alarming as regards pulmonary tuberculosis and its prognosis. The recognition of this manifestation, which many of the writers on the subject believe to be allergy, is important from the point of view of diagnosis of pulmonary tuberculosis and all that this means. No reference is made in this article to epituberculosis, the distinction of which from 'Löfller's syndrome' would appear to be difficult and perhaps to depend on whether or not an eosinophil count has been made.

Bronchostenosis.—L. E. Prickman and H. J. Moersch find that bronchostenosis is much commoner as a complication of allergic or infective asthma than is generally recognized. The lesion is described as a definite, localized stricture-like narrowing of a bronchus; it is regarded as primarily inflammatory and not due to allergic oedema or bronchial spasm. It was found in 29 males and 31 females, and clinically gives rise to paroxysmal cough, retention of bronchial secretion, and partial or complete collapse of the lung corresponding to the affected bronchus. Another symptom of bronchostenosis is the occurrence of febrile episodes; these occurred in 68 per cent of the authors' cases. It is pointed out that the diagnosis of broncho-pneumonia is not infrequently made. Bronchoscopic examination may show the narrowing of the bronchus, and the issue of purulent fluid from it may be visible; dilatation may be effected at the bronchoscopy by dilating forceps, and varying amounts of muco-purulent or purulent discharge may be aspirated. It is stated that if asthmatic patients with a history suggesting bronchial stenosis undergo bronchoscopy in the interval after they have recovered from the complication, visualization of the bronchi may not show any narrowing of the bronchi, although there is usually increased secretion or other evidence commonly present in chronic

asthmatic bronchitis. Only a relatively small number of asthmatic patients need bronchoscopy, namely, those in whom the presence of bronchial stenosis and its results seems possible.

Morbid Anatomy

Status asthmaticus

Fatality statistics.—B. Craig, Jun., discusses fatality during the status asthmaticus. This is rare: up to 1938 E. T. Thieme and J. M. Sheldon collected 43 recorded cases and added 7. Of 56,000 admissions to the Peter Bent Brigham Hospital, Boston, Mass., 1,378 represented those of 992 patients whose condition had been diagnosed as either primary or secondary bronchial asthma; of this number of cases 49 were fatal, and a necropsy was performed in 23; in 7 of these the clinical picture was that of the status asthmaticus without any extra pulmonary cause of death. These 7 cases are analysed clinically and pathologically. All were women from 24 to 67 years of age with an average of 45 years. The duration of the disease was from 6 months to 14 years. Clinically the heart was quite normal in 5; in 1 case the heart was enlarged, in the other the cardiac rate changed from 72 to 140. The pulse rate in the other cases was nearly always raised, usually between 100 and 140. The blood pressure was always normal, fever occurring in 4 cases; the blood showed a raised eosinophil count in 2 only, namely, 4 and 11 per cent.

Both to the naked eye and microscopically emphysema was constant. Microscopically the most severe lesions were seen in the middle-sized bronchi; in 6 cases thick plugs containing eosinophils were present; in 4 cases there were Curschmann's spirals noted, and also in 4 cases Charcot-Leyden crystals were found in the sputum in the bronchial tubes. In 6 cases the bronchial mucosa was thrown into folds and often there were small sacculations. The mucosa and submucosa were infiltrated with lymphocytes and eosinophils. The submucosal layer was always widened and the basement membrane thickened and hyaline. Hypertrophy of the bronchial muscles, present in all cases, varied from one bronchus to another. Distension of the mucous glands with inspissated mucus occurred in 5 cases. Treatment is difficult; 5 patients had previously responded to epinephrine, 1 patient had had a severe reaction, and 1 had never had it. Atropine was often used; in connexion with the thickening of the mucus due to atropine, it is pointed out that the patient showing the best Curschmann's spirals (twisted, compact concentrated bronchial plugs) had received 20 injections of atropine in her final illness.

Treatment

Peri-sympathetic injection

H. M. Wilensky reports on peri-sympathetic injection therapy in 18 cases of asthma. All the patients obtained some degree of relief, even though in some instances it was transient. Of 14 who received sufficient injections, 6, or 42.8 per cent, were completely cured; 4, or 28.6 per cent, were much benefited, i.e. attacks were greatly reduced in number and severity; and 4, or 28.6 per cent, obtained slight relief, i.e. the attacks were less frequent and milder. The technique is as follows: with the patient's back arched, a point is selected 4 centimetres from the spine and over the lower border of the rib above the interspace through which the injection is to be made. A few drops of a 2 per cent novocain solution are injected intradermally. A long security needle is then introduced perpendicularly to the inferior margin of the rib, and directed downwards and at an angle of 45° forward and inward for a distance of about 4 to 5 centimetres, instilling the anaesthetic ahead of the advancing needle. The needle is advanced a further 0.5 centimetre toward the spine, at which point about 2.5 cubic centimetres of absolute alcohol are injected. Possible complications are a sharp radiating pain around the chest, injury to the pleura with the production of a pneumothorax, and a mild intercostal neuralgia.

Aminophylline

Bronchial spasm.—R. H. Young and R. P. Gilbert report the effect of aminophylline for the control of bronchial spasm. They find that the drug appears to have a protective action against the broncho-constrictor activity of histamine. It seems that the beneficial effect of the drug in the relief of asthmatic attacks is due to its action directly on the bronchial musculature.

Theophylline mono-ethanolamine

R. W. Lamson and L. C. Bacon report on the use of theophylline mono-ethanolamine in 153 cases of asthma. Of these only about 10 per cent did not obtain relief. Doses of from 1 to 6 grains were given. Untoward reactions were slight, and tended to occur only during the first few doses of the drug. The authors consider that the drug may become a valuable adjunct to, if not a substitute for, ephedrine in the treatment of asthma.

Bohner, C. B., Sheldon, J. M., and Trenis, J. W. (1941) *J. Allergy*, **12**, 290.

Craig, B., Jun. (1941) *Arch. intern. Med.*, **67**, 399.

Freund, R., and Samuelson, S. (1940) *Arch. intern. Med.*, **66**, 1215.

Goldsmith, G. A., Ogaard, A. T., and Gowe, D. F. (1941) *Arch. intern. Med.*, **67**, 597.

Lamson, R. W., and Bacon, L. C. (1941) *J. Amer. med. Ass.*, **116**, 915.

Löffler, W. (1936) *Schweiz. med. Wschr.*, **66**, 1069.

Prickman, L. E., and Moersch, H. J. (1941) *Proc. Mayo Clin.*, **16**, 305.

Thieme, E. T., and Sheldon, J. M. (1938) *J. Allergy*, **9**, 246.

Turnley, W. H. (1941) *Arch. Otolaryng., Chicago*, **33**, 767.

Wilensky, H. M. (1940) *Canad. med. Ass. J.*, **43**, 59.

Young, R. H., and Gilbert, R. P. (1941) *J. Allergy*, **12**, 235.

ATHETOSIS

See also B.E.M.P., Vol. II, p. 212; Cumulative Supplement, Key No. 113.

Double or Bilateral Athetosis

Familial paroxysmal choreo-athetosis

Unusual syndrome.—L. A. Mount and S. Reback describe under the above title what is believed to be a hitherto unrecognized syndrome. There is a family history of 20 victims in 5 generations in 100 years; the great-grandfather, with whom the condition originated, lived to be 87. The transmissibility is apparently a non-sex-linked recessive hereditary characteristic. The attacks have never appeared in the siblings of unaffected parents. The patient, a man aged 23, was intensively studied for 2½ months at the Neurological Institute of New York and seen by most of the staff, none of whom had met with such a condition. Since infancy he had been subject to choreo-athetoid 'spells' which he divided into 'large' lasting up to 2 hours, and 'small' for 5 to 10 minutes, according to their severity and duration. The attacks were prone to occur before, during, or immediately after lunch; on three occasions attacks were produced by 90 cubic centimetres of whisky, thus suggesting a release of the lower motor centres from cortical control. Both forms of attack were preceded by an aura consisting of a tired feeling and stuffiness in the chest and throat; the aura was followed by 'a quick drawing-up' of either one or occasionally of both arms simultaneously, with adduction of the arm at the shoulder and flexion at the elbow and wrist, and at the same time there were slow, purposeless movements of the fingers in the form of irregular flexion, extension, and spreading. These movements were usually associated with supination of the foot on the same side, and sometimes diplopia. In the 'larger' attacks speech was dysarthric and at times anarthric. There was never loss of consciousness. At their height the choreo-athetoid attacks closely resemble those of Huntington's chorea. Emphasis is laid on the preliminary nature of this report and a further account is promised.

Mount, L. A., and Reback, S. (1940) *Arch. Neurol. Psychiat., Chicago*, **44**, 841.

ATHLETICS AND ATHLETIC INJURIES

See also B.E.M.P., Vol. II, p. 220; Cumulative Supplement, Key Nos. 114 and 115; and Surveys and Abstracts 1939, p. 235; 1940, p. 204.

Athletic Injuries

Joint injuries

Procaine injections for sprains.—J. Grieve reports on the use in 40 cases of sprained joints of procaine injections; 1.5 to 2 cubic centimetres of a 1 per cent solution were given into the area of maximal tenderness. If pain was relieved, a further 1 cubic centimetre was injected. Twenty-four hours later it was occasionally necessary to repeat the dose. After the first injection the injured part should be subjected to the normal ranges of movement.

Grieve, J. (1941) *Lancet*, **1**, 344.

AVIATION

See also B.E.M.P., Vol. II, p. 239; Cumulative Supplement, Key No. 116; Surveys and Abstracts 1939, p. 236; 1940, p. 205; and p. 29 of this volume.

General

Effects of flying

Hyperventilation.—In an article on the importance of hyperventilation in aviation by H. C. Hinshaw and W. M. Boothby, one of the authors (H. C. H.) mentions that the danger of this condition was brought forcibly to his notice during one of his earliest solo flights as a student pilot. While flying a light plane in turbulent air and attempting to calculate the landing manoeuvre, he began to feel faint, weak, dizzy, and anxious, but when a sense of tingling and numbness of the fingers was experienced, he realized that he had unconsciously induced hyperventilation. Although he was familiar with the clinical syndrome, he had never previously felt it while flying. A few minutes of controlled respiration brought about complete relief, and a satisfactory landing was made. Any normal person can readily experience the symptoms of hyperventilation by voluntary forced breathing; it is only necessary to force maximal inspiration and maximal expiration at an approximately normal rate. Within 30 to 60 seconds an odd sense of faintness and dizziness is noted. True rotary vertigo is not present, but an unsteadiness, described as light-headedness, is felt. Within a minute or two a characteristic numbness and tingling type of paraesthesia in the extremities is noted, panic and palpitation follow, the mind becomes clouded and consciousness is impaired. If forced breathing is continued for 5 minutes or longer, the muscles become tense, and carpopedal spasms occur. Air hunger may supervene, and if forced breathing is continued vasomotor collapse resembling shock may result. The more violent manifestations are rare in clinical practice and are seen only in hysterical subjects, but milder manifestations are common. It has been thought that some cases of effort syndrome may be due to hyperventilation, and that muscular cramps during swimming may be thus caused. Experienced pilots, when anxious

at low altitudes, may possibly be the subjects of hyperventilation, and 'freezing' to the controls may be due to the unconscious hyperventilation caused by fear.

Effect of altitude changes on intracranial volume.—M. N. Walsh describes observations made on a woman, aged 35 years, who had undergone a right temporal craniotomy for a supposed cranial tumour, and as a result had an extensive cranial defect; measurements of the intracranial volume were made by means of noting the elevation or depression of the scalp over the area of defect of bone when the woman was in a low-pressure chamber. During the period in which the pressure in the chamber corresponded to ascent in an aeroplane (diminution of atmospheric pressure) the scalp over the bony defect was raised above the level of the skull; at an altitude comparable to 28,000 feet, corresponding to a barometric pressure of 247 millimetres or about $\frac{1}{3}$ atmosphere, the scalp was elevated by 0.5 centimetre. During a period in which the pressure in the chamber was rising (as in a diving aeroplane) the area of scalp over the bony defect was sinking approximately to 1 centimetre below the level of the skull, and returned to the original level on again returning to atmospheric pressure at ground level. These observations obviously show a change in volume of the cranial contents which might be due in part to expansion of air in the cerebrospinal fluid in the ventricles or within the cranium, on ascent, as a result of diminished barometric pressure, and compression of the air volume inside the cranium with increased barometric pressure. It is possible that these changes, resulting from considerable alterations in barometric pressure, were due wholly or in part to variations in the amount of blood in the capillaries and veins or to an alteration in the amount of free cerebrospinal fluid within the cranium.

Peptic ulcer in pilots.—J. H. Tillisch reports a case of haemorrhage from a duodenal ulcer in a pilot, aged 29, while flying. On account of the nature of aviation and the type of individual attracted to it, a higher incidence of peptic ulcer might be expected among pilots than in the average population. This proves to be true; in routine examination of 103 transport pilots at the Mayo Clinic, 5 were found to have a duodenal ulcer. With the progress of time the incidence of peptic ulcer in this group will increase.

Examination of the Special Senses

Intra-ocular pressure at high altitudes

Experimental investigation.—E. A. Pinson investigated on anaesthetized rabbits the condition of the intra-ocular pressure during exposure at altitudes from 1,000 to 40,000 feet. For this purpose a manometric system was devised with a capillary mercurial manometer, in order to measure intra-ocular pressures in terms of pressure above outside environment or barometric pressures, irrespective of changes that would occur as the altitudes were altered. The conclusion reached from these experiments was that the environmental pressure changes did not produce any alterations in the intra-ocular pressure sufficient to cause injury or discomfort in the eyes.

Audiometric tests

Incidence and types of deafness.—P. N. Pastore reports the results of audiometric tests of 88 out of 100 experienced pilots employed by one of the largest commercial air lines in the United States. The ages of the pilots ranged from 22 to 40 years, and their flying time from 8 months to 17 years. Sinusitis, which Brouwer of Belgium in 1935 regarded as a true occupational disease, was noted in 2 cases only. Of the 88 pilots 42, with an average of 4 years' flying, were normal as regards hearing, and 5 had so-called border-line normal hearing; 16 had nerve deafness, 3 unilateral conduction loss, and 22 conduction type of loss. The zone in which the largest number of pilots were found to have a deficiency in hearing was that of the 4,096 cycle area; the tones 128 to 2,048 were hardly affected. This investigation indicates that pilots vary in the way that they are affected by exposure to noise. Of the 16 pilots with the perception or nerve type of diminished hearing loss, only one was conscious of some change in his hearing, and he gave a history of familial deafness. Among the 22 pilots with the air conduction type of diminished hearing the zone of greatest loss was that of the 4,096 cycle note. As yet there has not been any universal adoption of one of the ear protectors suggested.

Diseases Associated with Aviation

Deafness

P. A. Campbell and J. Hargreaves state that the deafness of aviators may be classified according to the aetiology, as follows: (1) acute fatigue of the end-organs of hearing and related structures; (2) chronic accumulative fatigue of the end-organ and related structures; (3) chronic changes of pressure in the middle ear inherent with changes in altitude, if ventilation of the middle ear is faulty; (4) chronic conduction deafness due to alteration in tissue resulting from faulty ventilation of the middle ear. Fatigue of the end-organ of hearing is due to noise and the effect of other vibratory energies inherent in flight. Altitudinal decrease in oxygen may be a factor in the production of fatigue.

Campbell, P. A., and Hargreaves, J. (1940) *Arch. Otolaryng., Chicago*, **32**, 417.

Hinshaw, H. C., and Boothby, W. M. (1941) *Proc. Mayo Clin.*, **16**, 211.

Pastore, P. N. (1941) *Proc. Mayo Clin.*, **16**, 214.

Pinson, E. A. (1940) *Aviation Med.*, **11**, 108.

Tillisch, J. H. (1941) *Proc. Mayo Clin.*, **16**, 209.

Walsh, M. N. (1941) *Proc. Mayo Clin.*, **16**, 220.

BACKACHE AND LUMBAGO

See also B.E.M.P., Vol. II, p. 251; Cumulative Supplement, Key No. 117; and Surveys and Abstracts 1939, p. 238; 1940, p. 207.

Abnormalities*Spondylolisthesis*

Fourth lumbar vertebra.—W. M. E. Topping records 2 cases of spondylolisthesis of the 4th lumbar vertebra in labourers, aged 52 and 59 years, and reviews this subject which has been so much more widely recognized as the result of radiological examination. It is pointed out that spondylolisthesis of vertebrae other than the 5th lumbar is sufficiently rare to justify publication. Radiologically the underlying morbid change in these 2 cases was the same as that in the usual site of spondylolisthesis, namely, the 5th lumbar vertebra. There was not any disability attributable to the vertebral displacement, and there was not any history of injury. Reference is made to Friberg's review of 302 cases of spondylolisthesis diagnosed in Sweden from 1927 to 1938, in 280 of which the defect in the interarticular portion was shown radiologically. In his own series Friberg found the condition in 44 per cent, and the 4th lumbar vertebra to be involved in 23 per cent.

Friberg, S. (1939) *Acta. chir. Scand.*, **82**, suppl. IV.

Topping, W. M. E. (1941) *Brit. J. Radiol.*, N.S., **14**, 162.

BITES AND STINGS

See also B.E.M.P., Vol. II, p. 343; and Surveys and Abstracts 1939, p. 241.

Arthropoda*Arachnida*

Scorpions.—P. K. Rao recommends the injection of 2 cubic centimetres of a sterilized 2 per cent solution of sodium bicarbonate for the treatment of scorpion stings. The solution should be infiltrated all round the area of the sting. If the pain does not subside within a few minutes, the injection should be repeated. This treatment was employed in 84 cases of scorpion sting with invariably good results.

Rao, P. K. (1941) *J. Indian med. Ass.*, **10**, 154.

BLADDER DISEASES

See also B.E.M.P., Vol. II, p. 374; and Surveys and Abstracts 1939, pp. 34 and 242; 1940, p. 207.

Stone*Anuria*

Due to sulphapyridine calculi.—J. F. Sadusk, L. Waters, and D. Wilson report 2 cases of anuria caused by sulphapyridine calculi. In both cases the anuria was due to the calculi blocking the urinary tract at the uretero-vesical orifices. Treatment, which was successful, consisted of cystoscopy and catheterization of the ureter, and lavage of the renal pelvis and ureter with warm distilled water until urine dripped from the catheter and retrograde pyelograms showed a clearly outlined upper urinary tract.

Foreign Bodies*Urethral catheter*

L. H. Baretz reports the case of a woman, aged 30, who complained of bilateral lower-quadrant pain, frequency, dysuria, and haematuria of 3 months' duration. Radiography showed an S-shaped calcified shadow in the bladder; the upper end of the shadow emerged into the abdominal cavity. Suprapubic cystotomy showed a urethral catheter which penetrated the vault of the bladder. The intravesical portion of the catheter was coated with a white incrustation of phosphatic salts. The catheter had apparently been introduced 4 years previously to induce abortion. The patient recovered uneventfully after removal of the catheter.

Nervous Diseases*Urinary retention*

Treatment by β -methylcholine urethane.—Various derivatives of choline are now used therapeutically, on account of their parasympathomimetic action. Acetylcholine is rapidly destroyed in the body. Acetyl- β -methylcholine chloride (mecholyl) is used clinically, as also is carbamylcholine chloride (carbachol, doryl, moryl, choryl). I. Starr and L. K. Ferguson tested the effects on both healthy volunteers and patients, altogether 150 individuals, of a new compound resembling doryl, namely, carbaminoyl- β -methylcholine, also properly called β -methylcholine urethane or B.M.C.U. Its action is weaker than that of doryl and the dose is about 10 times greater, but it is also less toxic. Because of the toxic side effects of doryl the authors strongly recommend substitution of this compound in certain clinical conditions. Subcutaneous injection of 2 to 10 milligrams in 22 healthy medical students did not cause any undesirable reactions. Oral administration to 20 subjects, who received between 2 and 24 milligrams daily in divided doses, was also free from unpleasant effects. The chief therapeutic value of the drug is in post-operative urinary retention. To relieve retention B.M.C.U. was given hypodermically in doses of 2 milligrams. In the absence of relief within 20 or 30 minutes, the dose was repeated once, twice, or even three times. In 122 attempts to relieve post-operative urinary retention, the drug was successful in 82 cases, or 68 per cent; 37 voided after the first

dose, 35 after the second, 8 after the third, and 2 after the fourth dose. Undesirable side effects can be completely relieved by the administration of atropine sulphate, $\frac{1}{50}$ grain, subcutaneously, after which massage should be given at the site of injection. In the treatment of abdominal distension and of peripheral vascular disease, the authors consider that B.M.C.U. has not any advantages over other forms of treatment and there was not any evidence that the drug was of value in either hypertension or paroxysmal tachycardia.

After spinal anaesthesia.—E. L. Peirson and C. F. Twomey report the case of a man aged 60 who was quite well until appendicectomy was performed under spinal anaesthesia. The operation was followed by complete retention of urine for $2\frac{1}{2}$ months. As a complete study of the case failed to show any other cause of retention, it was assumed that this was due to nerve injury resulting from the spinal anaesthesia. Presacral nerve resection relieved the retention, and the patient had, until the time of the report, remained well.

Baretz, L. H. (1941) *Urol. cutan. Rev.*, **45**, 186.

Peirson, E. L., and Twomey, C. F. (1940) *New Engl. J. Med.*, **223**, 171.

Sadusk, J. F., Waters, L., and Wilson, D. (1940) *J. Amer. med. Ass.*, **155**, 1968.

Starr, I., and Ferguson, L. K. (1940) *Amer. J. med. Sci.*, **200**, 372.

BLINDNESS

See also B.E.M.P., Vol. II, p. 407; Cumulative Supplement, Key Nos. 149–162; and Surveys and Abstracts 1939, pp. 128 and 244; 1940, p. 210.

Degenerations and Optic Atrophy

Degenerations of the retina

Incomplete Laurence-Moon-Biedl syndrome.—R. W. B. Ellis and F. W. Law record the case of a girl, aged 13 years, with infantilism, obesity, and retinal dystrophy, as an incomplete form of the complete Laurence-Moon-Biedl syndrome. Her parents were not related, but features of the syndrome lacking in the girl, namely, mental defect and polydactyly, were present in a sister and uncle. She was a perfect example of infantilism associated with obesity; although her intelligence was normal for her age, her emotional development corresponded with her physical state. There was not any resemblance between the retinal changes in the patient and those typical of retinitis pigmentosa, and in this respect the present case resembles the first case recorded by Laurence and Moon in 1866, and only in 15 per cent of the recorded cases have the appearances been those of typical retinitis pigmentosa.

Optic atrophy

Tryparsamide therapy in primary atrophy.—H. Sutherland-Campbell, in a review of the use of tryparsamide in primary optic atrophy, concludes that its use is not justifiable. Of the reported cases only a relatively small number are concerned with the treatment of primary optic atrophy with the drug without damage to the optic system. Three of the reports indicate that there was improved vision in a few cases. In the other 4 reports dealing with the great majority of cases, the harmful effects of the drug in the presence of primary optic atrophy is emphasized in practically all cases; it appears that most authors consider that the use of tryparsamide is not justifiable.

Vascular and Blood Diseases

Haemorrhage

Disease of the blood-forming tissue.—H. L. Tidy reviews the occurrence of blindness after haemorrhage. A distinction is drawn between immediate momentary blindness, probably due to withdrawal of blood from the cortical visual centres, and delayed blindness, which may be permanent. Previous reports on the subject contain 18 cases only of such blindness from 1912 to 1924. It never occurs in cases of haemorrhage alone in otherwise normal subjects, nor in anaemia alone, though 2 cases of visual interference have been reported out of 117 cases of pernicious anaemia between 1911 and 1920. Recurrent blood-letting was formerly a frequent cause of blindness. The sites of haemorrhage in the cases reported are most often peptic ulcers and epistaxis. Three cases of blindness in the war of 1914–18 arose from amputation of the lower limb accompanied by gas gangrene. Age and sex appear to be irrelevant factors. The blindness is usually bilateral. Recovery is gradual and varies in length. Blindness was complete and permanent in 33 per cent of the cases reported, partial and permanent in 5 per cent, and good recovery was made in 10 per cent of the cases. Visual field findings show central or paracentral scotomas with enlargement of the blind spot and slight contraction of the colour field. Ophthalmological changes are inconstant. They have been compared by Goerlitz to those due to intoxication amblyopia. Local oedema is an important factor in pathological lesion. Degeneration of the ganglion cells of the retina and retrobulbar neuritis have been suggested as causes of blindness. The author describes a recent case of a woman aged 30, anaemic since childhood. The patient had considerable loss of blood in childbirth and had oedema of the feet. After treatment for anaemia, blindness developed accompanied by central scotomas and swelling of the disks. Vision was fully recovered in 4 months.

C. H. Bamford and H. Barber report a case of blindness after haematemesis in a man aged 46 years. After two severe attacks of bleeding within 3 days, he noticed 2 days later that his sight was failing and gave a clear description of a gradual concentric contraction of the fields of vision. Four days later he was completely blind. On examination the pupils were widely

dilated and inactive to light, there was severe oedema of the retina at the posterior pole, with swelling of both optic disks.

Bamford, C. H., and Barber, H. (1940) *Lancet*, **2**, 715.

Ellis, R. W. B., and Law, F. W. (1941) *Arch. Dis. Childh.*, **16**, 105.

Sutherland-Campbell, H. (1940) *Arch. Ophthalm.*, N.Y., **24**, 670.

Tidy, H. L. (1941) *Brit. med. J.*, **1**, 774.

BLOOD EXAMINATION

See also B.E.M.P., Vol. II, p. 457; Cumulative Supplement, Key Nos. 163–169; Surveys and Abstracts 1939, pp. 21, 52, and 245; 1940, pp. 113, 119, 137, and 210; and p. 6 of this volume.

Physical and Chemical Changes

Sedimentation of red cells

In malignant disease.—H. Feldman has repeated and confirmed the observations of L. Koster who found a maintenance of the serial sedimentation rate of the red cells in 95 per cent of 112 cases of malignant disease and in all of 14 cases of Hodgkin's disease. In 100 normal persons and 460 morbid conditions other than malignant disease, the sedimentation rate was not maintained, but declined steadily *in vitro*. Feldman during 2½ years carried out this sedimentation rate in 176 cases; of these 118 were proved to be malignant, including three of Hodgkin's disease. All except 51 gave a positive maintenance sedimentation rate. Of the 55 cases of non-malignant disease 52, or 94·6 per cent, gave a negative reaction. It is hoped that this maintenance sedimentation test may eventually help in the diagnosis of malignant disease; but some questions remain to be answered, such as the basis of the test, and especially the influence of drugs, such as potassium iodide, bismuth, salvarsan (Koster), sulphanilamide, and sulphapyridine (Feldman).

Chemical analysis

Russell's viper venom technique.—H. W. Fullerton describes a simplified method of estimating prothrombin by employing the venom of Russell's viper as the thrombokinase. The technique is exactly the same as that of Quick (1938), except for the following points: (1) 0·2 cubic centimetre each of plasma, calcium solution, and thrombokinase solution are used, instead of 0·1 cubic centimetre as in Quick's method; (2) stypven solution, instead of tissue extract, is used as the thrombokinase, 0·1 milligram of the venom being dissolved in 1 cubic centimetre of distilled water immediately before use.

Blood electrolytes and the menstrual cycle.—It has been shown by urinary examination that sodium chloride and water are retained during the intermenstrual and premenstrual phases of the cycle and that the onset of menstruation is associated with their increased excretion (G. W. Thorn, K. R. Nelson, and D. W. Thorn). E. M. P. Eckstein, M. Lubran, and T. McKeown publish the results of an investigation to determine if significant changes occur in the blood electrolytes in normal women and, if so, whether or not these could be interpreted in relation to the menstrual cycle. Observations were made on 5 normal women with an average age of 23½ years, for about 2 months. The variations in the levels of the blood sodium and chloride appeared to be directly correlated with the menstrual cycle. These electrolytes are retained during the first half of the cycle; after this time the levels in the blood begin to fall. No constant relation was shown between the level of the serum potassium and the stage of the cycle.

Low blood diastase.—S. H. Gray, J. G. Probststein, and C. J. Heifetz report on some observations made at the Jewish Hospital at St. Louis on the blood diastase during the years 1933–8. A compilation of the diastase levels made in 410 cases of disease of biliary tract included those determined in (1) 235 cases of diseases of the liver and bile ducts and (2) in 175 cases of diseases of the gall-bladder. A comparison of the two groups shows that a higher percentage of subnormal levels is found in cases of disease of the liver and bile ducts. Acute cholecystitis showed a much lower level than did chronic cholecystitis; in both generalized and local infection involving the liver, the blood diastase level was lowered. In 141 cases of pneumonia (lobar 36, broncho-pneumonia 105) the blood diastase was generally lower than in any other infection, the greater the toxicity the greater the fall. In diabetes mellitus discordant results have been found by others. Among 736 cases there was a tendency for the blood diastase to fall to a low normal or subnormal level; on the whole the more severe the diabetes mellitus the lower the diastase level of the blood. In eclampsia, hyperthyroidism, drug poisoning, and chloroform anaesthesia the level also tends to be low. The same workers contribute a paper on the significance of a high level of blood diastase. This was long ago held to occur exclusively in pancreatic disease, but it is now known that elevated levels may also be obtained in impaired renal function, in perforation of a posterior peptic ulcer into or close to the pancreas, and in some acute disease of the salivary glands, parotitis, and mumps. It has now been shown that in pancreatic disease a high level occurs only in the acute phase and lasts a short time only. Chronic lesions, such as tumours, either have no effect at all or produce a rise only when there is a sudden acute involvement of previously unaffected pancreatic tissue, for example, carcinoma of the pancreas might be present in its early stages without causing any change in the blood diastase. But as the lesion spreads there might be fairly rapid occlusion of a pancreatic duct or artery resulting in a sudden rise of the diastase level, which would be followed by a return to the previous level.

- Eckstein, E. M. P., Lubran, M., and McKeown, T. (1940-41) *Guy's Hosp. Rep.*, **90**, 28.
 Feldman, H. (1940) *Amer. J. med. Sci.*, **200**, 820.
 Fullerton, H. W. (1940) *Lancet*, **2**, 195.
 Gray, S. H., Probst, J. G., and Heifetz, C. J. (1941) *Arch. intern. Med.*, **67**, 805.
 Heifetz, C. J., Probst, J. G., and Gray, S. H. (1941) *Arch. intern. Med.*, **67**, 819.
 Koster, L. (1937) *Acta. med. scand.*, **93**, 420.
 Quick, A. J. (1938) *J. Amer. med. Ass.*, **110**, 1658.
 Thorn, G. W., Nelson, K. R., and Thorn, D. W. (1938) *Endocrinology*, **22**, 155.

BLOOD PRESSURE, HIGH AND LOW

See also B.E.M.P., Vol. II, p. 503; Cumulative Supplement, Key Nos. 170 and 171; Surveys and Abstracts 1939, pp. 19, 56, and 248; 1940, p. 211; and p. 2 of this volume.

Clinical Estimation of Blood Pressure

The auscultatory method

M. R. Berry discusses the mechanism and prevention of impairment of the auscultatory sounds during determination of blood pressure in individuals standing up, a procedure practised in the examination of those suspected to be the subject of orthostatic low blood pressure. In examination by the auscultatory method of persons standing up the sounds heard by the stethoscope may become indistinct or even inaudible, so that the diastolic pressure cannot be determined. This impairment of the auscultatory sounds is due to venous congestion distal to the cuff of the sphygmomanometer. If the arm of the standing person is raised above the head so that the veins become comparatively empty of blood and if the cuff of the sphygmomanometer is then inflated so as to reach a pressure above the systolic level, and the arm is then lowered, the impairment of the auscultatory sounds is prevented and the estimation of blood pressure is much simplified. The phenomenon of the 'auscultatory gap', occasionally found in hypertensive patients, consists of the disappearance and reappearance of the intermediate auscultatory sounds between systolic and diastolic values for blood pressure. In 2 such cases drainage of the venous reservoir, as described above, before the blood pressure was taken, was followed by continuous auscultatory sounds between the systolic and diastolic value for blood pressure.

Influence of doctor on hypertensive patients

D. Ayman and A. D. Goldshine continue their observations on the lower arterial blood pressure when taken at home by the hypertensive patient or one of his family, and when taken by a medical practitioner at the hospital or the consulting room. The blood pressure taken in the home by the medical man is the same as that estimated by him at the hospital or consulting room. It is apparently impossible for the hypertensive patient to become immune to the pressor influence exerted by the presence of a medical practitioner; it is as constant as that of cold or breath-holding. Further, it is stated that the pressor effect of the medical man may counteract the hypotensive effects of drugs or operations which in the past have been regarded as devoid of any hypotensive influence, and that these should be examined again under home conditions.

High Blood Pressure

Essential hypertension

Supradiaphragmatic splanchnectomy.—F. T. Tooke and J. V. V. Nicholls report 15 cases of malignant hypertension treated by supradiaphragmatic splanchnectomy. From every point of view, including that of the fundus oculi, 2 patients were cured, 3 were markedly improved, 8 moderately improved, and 1 unchanged. Of all the changes noted, the improvement in the fundus findings and visual acuity were the most notable.

In childhood.—I. P. Sobel reports 7 cases of so-called essential hypertension in childhood. Transitory or intermittent elevations of blood pressure to hypertensive levels in children and adolescents should not be disregarded, as they may point to the development of permanent hypertension later in life. The hypertensive state in adult life often has its origins in childhood. It may be detected at this time by utilizing frequent routine determinations of blood pressure and by the cold pressor test in the study of both children and their parents.

D. Court reports a case of malignant hypertension in a girl aged 10 years, and collects records of 11 cases published during the last 12 years under the ages of 14 years, with an average age of 10 years, in 4 males and 8 females. Analysis of the 12 cases showed that headache, vomiting, and papilloedema occurred in all; visual disturbance in 8; haemorrhage, especially haematuria, in 7; and convulsions in 6. These signs and symptoms are associated with severe and progressive hypertension for which no cause can be found, though the angiospasm is more probably humoral than nervous in origin. The average highest systolic blood pressure in the 12 patients was 230 millimetres of mercury, and the average highest diastolic blood pressure 160 millimetres of mercury. The disease is invariably fatal, the maximal duration being 5 years, and the minimal 6 months. The disease is generalized throughout the vascular system and shows hypertrophy of the cardiac ventricles and can be demonstrated by biopsy of the voluntary muscles. The renal arterioles undergo proliferation of the intima

leading to obliteration (endarteritis fibrosa, Ellis) and acute fibrinoid necrosis involving the glomerular tufts in the kidneys.

Aetiology.—A. C. Corcoran and I. H. Page state that angiotonin (or renin when acted upon by its activator) when injected into animals produces the effects characterizing arterial hypertension in man, namely, cardiac enlargement, arteriolar constriction, and constriction of the renal arterioles. This suggests that possibly angiotonin is involved in the pathogenesis of essential hypertension and malignant hypertension in man. The endocrine system, particularly the adrenal cortex and hypophysis, appear to participate indirectly in some forms of hypertension in man, in whom the high state of nervous organization may even make it a very powerful factor.

Degrees of fluctuation.—G. E. Mountain and E. V. Allen confirm and emphasize the wide fluctuations of blood pressure which may occur in the subjects of essential hypertension in contrast to the rather narrow limits of fluctuation seen in those with a normal blood pressure. This was noticed in 1920 by J. P. O'Hare, who saw the systolic blood pressure fall from 270 to 110 millimetres of mercury after administration of glyceryl trinitrate. They also compared spontaneous reductions of blood pressure with those induced by drugs and by pressure on the carotid sinus, and investigated the relation of the groups of hypertension (the four groups described by N. M. Keith, H. P. Wagener, and N. W. Barker) to fluctuations of blood pressure and to the degree with which blood pressure approaches normal in hypertension. From examination of 228 hypertensive patients it was found that there was an average variation of 49 millimetres of mercury in the average systolic, and of 35 millimetres of mercury in the average diastolic blood pressures. But the four groups of hypertension cases, which were based on retinal findings, differed in the character of the blood pressures; thus in group 1 hypertension the fluctuation was comparatively slight because the hypertension was not severe; in groups 2 and 3 the blood pressure was higher and the fluctuations more prominent. In group 4, the worst from a prognostic point of view, the fluctuation was slightly less than in hypertension group 1 because the blood pressure was relatively fixed at a high level. The authors confirm the conclusion that the less closely the blood pressure approaches normal as a result of rest and sleep, the more serious the condition.

Hypertension associated with renal disease

Value of chemotherapy.—R. M. Nesbit and R. K. Ratliff quote experimental and clinical observations showing that arterial hypertension may result from renal lesions which may be bilateral or unilateral. The three different types of unilateral renal lesion most often associated with hypertension are those due to gross vascular occlusion of the renal arteries including trauma to the kidney, obstructive uropathies, and chronic inflammatory lesions. As chronic infection appears to be the most important single aetiological factor, it would appear that the best treatment of this type of hypertension is prophylactic. The value of modern chemotherapy in this connexion is great. In unilateral nephropathy the removal of the diseased kidney often leads to improvement, provided that the function of the other kidney is not greatly reduced.

Metabolic activity of the kidneys.—According to S. Rodbard and L. N. Katz, the chemical mediator of renal hypertension is rapidly destroyed by the metabolic activity of the normal kidney. The excretory function of the kidney plays little, if any, part in eliminating the mediator of hypertension. Any specific substances which might be responsible for the uraemic syndrome are neither produced nor eliminated to any significant extent by the metabolic activity of the kidneys. The elimination of these uraemia-producing substances would have to be primarily dependent upon the excretory activities of the kidney.

Pyelonephritis.—S. Weiss and F. Parker, Jun., state that pyelonephritis sometimes becomes chronic and leads to arterial hypertension and to renal or cardiac insufficiency. The authors report a case in which the renal infection began at the age of 6 months and lasted until the patient's death at the age of 15; although the local symptoms with pyuria were prominent in childhood, chronic nephritis with hypertension was the presenting syndrome in later years.

W. F. Braasch and C. E. Jacobson studied 180 cases of chronic bilateral pyelonephritis in order to ascertain the part played by this infection in the aetiology of hypertension. Hypertension was considered to be present if the systolic blood pressure exceeded 145 millimetres of mercury or the diastolic 90 millimetres of mercury. The cases were divided into three groups: in group 1 were 50 cases in which renal symptoms had been present for from 1 to 5 years; in group 2 were 50 cases in which symptoms had been present for from 5 to 10 years; and in group 3 were 80 cases in which symptoms had been present for 10 years or more. Of the 180 cases, 47, or 26 per cent, were hypertensive. In a normal control series of 975 cases the incidence of hypertension was 20 per cent. In groups 1, 2, and 3 the incidence of hypertension was 22, 26, and 29 respectively; in each age group the incidence of hypertension was higher among the patients with pyelonephritis than among those in the control group.

Unilateral atrophic pyelonephritis.—R. L. J. Kennedy, N. W. Barker, and W. Walters report a case of malignant hypertension in a girl aged 7 years, due to unilateral atrophic pyelonephritis. The blood pressure varied between 225 millimetres of mercury systolic and 178 millimetres of mercury diastolic and 170 millimetres of mercury systolic and 110 millimetres of mercury diastolic. The ocular fundi showed acute angiospastic retinitis. The condition, at the time of the report, had been cured for 3 months by removal of the diseased kidney. The blood pressure had fallen to 108 millimetres of mercury systolic and 74 millimetres of

mercury diastolic, and the changes in the ocular fundi had subsided to a point at which complete recovery appeared to be assured.

N. W. Barker and W. Walters report the study of 4 cases in which hypertension was associated with unilateral chronic atrophic pyelonephritis. In these cases, after surgical removal of the diseased kidney, there was a return of the blood pressure to within normal limits, and its persistence within such limits; hypertension was of varying degrees of severity, but in no case was there evidence of advanced organic arterial damage. In all cases the diastolic blood pressure was relatively higher than the systolic (e.g. 170/110 millimetres of mercury). In all cases the removed kidneys were markedly contracted, and each weighed less than 75 grammes, or less than half the normal weight.

Treatment of renal hypertension with depressor renal extract.—A. Grollman, J. R. Williams, and T. R. Harrison, on the grounds that recent experimental work has clearly indicated that there is a rational and logical basis for the possible therapeutic value of renal extract in hypertension of renal origin, prepared extracts of kidney which, when administered orally to normal animals, did not produce a decline in blood pressure, but had the property of partially inhibiting the pressor effect of subsequently injected renin. When extracts containing the renal anti-pressor substance in sufficient amount were given orally or parenterally to animals with experimental renal hypertension, a decided and prolonged decline in blood pressure occurred. The extract was tried clinically in a small number of patients, being given orally or parenterally, and in most cases a fall in blood pressure occurred. The available evidence is held by the authors to indicate that the renal anti-pressor substance has certain unique properties which differentiate it from various depressor tissue extractives described by previous investigators.

Effect of nephrectomy on the pressor response to renin.—A. Freedman reports on the effect of nephrectomy on the response to renin in unanaesthetized rats. These rats were found to be abnormally sensitive to the pressor effects of renin, both as to degree and duration. The blood pressures of the normal rats rose on an average 30 millimetres of mercury within 4 to 7 minutes after the injection of renin, whereas in nephrectomized rats it was 58 or nearly double the millimetres of mercury. After the prompt initial rise the blood pressures of the normal fell to about pre-injection levels in 2 to 3 hours, whereas the return to normal in nephrectomized rats was delayed for 5, and often 12, hours. An average of the blood pressure levels during the period from 4 to 12 hours after nephrectomy was 39 millimetres of mercury above the pre-injection level, whereas the blood pressure of the rats with intact kidneys was almost normal. The intact kidney, from which the pressor substance, renin, is extracted, appears to possess the property, *in vivo*, of counteracting, in some manner, the effect of this same substance when it is artificially injected.

High Blood Pressure in General

Course and Prognosis

Relation to body build.—S. C. Robinson and M. Brucer review at considerable length the divergent opinions about the relation between physical conditions of the body and the occurrence of arterial hypertension; for example, in a statistical analysis of 6,000 prisoners and 400 prison guards. W. C. Alvarez and L. L. Stanley (1930) concluded, contrary to general impression, that there is not any correlation between a thick-set stocky body build and arterial hypertension. Robinson and Brucer analysed the periodical health examination records, conducted by the Life Extension Insurance examiners in the Chicago office, of 3,658 (males 1,861, females 1,797) unselected persons. Of the males 17 per cent and of the females 31 per cent were of the narrow-chested linear type, whereas 12 per cent of both males and females were of the broad-chested lateral type of body build. In both males and females of the lateral or broad-chested type there was an increased liability to hypertension. Among these males there was more than four times the expectancy of systolic hypertension and seven times the expectancy of diastolic hypertension as have the males of the slender or linear build; females of the lateral build have almost eleven times the expectancy of systolic hypertension and eight times that of diastolic hypertension among the females of the linear build. Males and females of lateral build have an expectancy of a low systolic or diastolic pressure only about one-half of that of males and females of slender linear build. The relation between lateral build and hypertension and between linear build and low blood pressure is found in all age groups. The incidence of high pressures increases and low pressures decreases with age in males of lateral build; in males of linear build the incidence of high pressure is constant up to the seventh decade and the incidence of low pressure is constant throughout life. The incidence of high pressures increases with age more prominently among females of lateral build than among those of linear build and at every age the incidence of hypotension is greatest among females of linear build.

Low Blood Pressure

Clinical picture

Postural hypotension: a disease of the sympathetic nervous system.—E. A. Stead, Jun., and R. V. Ebert report on the observations made by them on 3 men, aged 56, 58, and 72, with pronounced postural hypotension. The subjects were examined with the help of a tilted table, a mercurial sphygmomanometer to take the arterial pressure at the level of the heart; the blood-flow in the hand and foot was measured by plethysmographic methods, the hands and feet

being in the plethysmographs at a constant temperature for at least 30 minutes before observations were made. The basal blood volume was determined by the method of J. G. Gibson and W. A. Evans as adapted to the photo-electric micro-colorimeter. This method, combined with the application of arterial tourniquets, was used for the measurement of the volume of blood in the lower extremities with the subject in the horizontal and in the standing positions. When the subjects were placed on the tilt table and tilted upright the arterial blood pressure fell rapidly, but signs or symptoms of impaired cerebral function did not appear until the systolic pressure fell below 50 millimetres of mercury and sometimes systolic pressures as low as 40 millimetres of mercury were tolerated for 10 to 15 minutes without any obvious loss of mental acuity. The first signs of diminution of the supply of blood to the brain were slight pallor, blurring of vision, tremor of the hands, and inability to understand directions; there was not any sweating or abdominal discomfort. If the motionless standing position was continued, generalized clonic movements of the arms and legs without tonic spasms occurred. When the subject was returned to the horizontal position, consciousness was at once restored, and the blood pressure rapidly returned to its resting level, but there was not any recollection of events during the latter part of the standing period. The effect of the application of tourniquets to both thighs was important: with the subject in the horizontal position pressure cuffs were placed on the proximal parts of both thighs and inflated suddenly from a large reservoir to a pressure of 250 millimetres of mercury. The subject was then tilted to an angle of 60° to 75°, and the arterial pressure was maintained at a level much higher than before the tourniquets were applied; on release of the tourniquets with the subject still in the standing position loss of consciousness and clonic movements occurred before the level of the arterial pressure could be taken. These observations confirm those of other workers, and show that in the upright position pooling of blood in the abdomen alone does not produce a striking fall of arterial pressure. Further investigations clearly indicate that pooling of blood in both the abdomen and the lower extremities is necessary to produce the fall of arterial pressure that occurs in the upright position. The cardiovascular reactions of the subjects with postural hypotension differ in several respects from those of normal individuals whose postural adaptations have been temporarily deranged by sodium nitrite, infections, or haemorrhage. In postural hypotension the rate of the heart is unchanged or shows a moderate increase as the arterial pressure falls. Hypotensives are free from symptoms while standing as long as the arterial pressure remains at or over 50 millimetres of mercury, whereas normal subjects are often uncomfortable when the arterial pressure falls from 120 to 90 millimetres of mercury and are markedly affected when it falls to 80 or 70 millimetres of mercury. Syncope occurs in hypotensives with less pallor and discomfort than in normal persons. Postural hypotension is regarded as a disease of the sympathetic nervous system, but it cannot be definitely stated whether the central or peripheral portion is involved.

Pathology

Post-operative hemiplegia.—A. D. Ecker and M. Deren record the occurrence of post-operative fatal hemiplegia associated with, and possibly due to, a fall of blood pressure in 3 arteriosclerotic men aged 61, 77, and 88 years. Necropsies showed wide-spread areas of partly haemorrhagic necrosis in the cerebral cortex with little involvement of the subjacent white matter, and pin-point but no large haemorrhages. Thrombosis of pial but not of large arteries or veins was present.

Systolic and diastolic pressures

Incidence and aetiology.—S. C. Robinson, who in 1939 with M. Brucer analysed the range of normal blood pressure among 10,883 urban inhabitants, now argues that hypotension is an ideal blood pressure level and not a disease. The dividing line between the normal and hypotensive pressure has never been unanimously agreed on; the upper limit of systolic hypotension has been put as high as 120 millimetres of mercury, and as low as 90 millimetres of mercury. About half the observers have chosen 110 millimetres for the upper limit of the hypotensive systolic pressure, and for the diastolic pressure 70 millimetres of mercury has been selected by Robinson. Among the 10,883 persons 25 per cent showed hypotensive systolic pressure and 34 per cent hypotensive diastolic pressure. It seems to be generally agreed that the incidence of hypotension among the population is 20 per cent. The occurrence of a systolic pressure below 90 millimetres is rare: of 7,478 men 42, or 0.5 per cent only, and of 3,405 women 56, or 1.7 per cent only. Those with hypotension, both males and females, tend to be underweight. Slender-built men and women are more often hypotensive than broad-built men and women. An annual study of blood pressure readings for 5 to 10 years showed that the year-to-year variation in blood pressure was much less among those who consistently registered low pressure than among hypertensives. Hypotension tends to maintain an even level, not to rise with advancing years. Hypotension is associated with a mortality rate lower than that of average blood pressures. The commonly accepted characters of hypotensives 'not exactly ill, yet rarely well', fatigue, headache, and dizziness are wide-spread and are commoner in hypertensives. In fact there are not any symptoms peculiar to or due to hypotension.

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BLOOD TRANSFUSION

See also B.E.M.P., Vol. II, p. 530; Cumulative Supplement, Key No. 172; Surveys and Abstracts 1939, p. 250; 1940, pp. 34 and 217; and pp. 8, 38, and 97 of this volume.

Technique of Transfusions

Apparatus and procedure

Clots in apparatus.—A. M. Giles devised the following method of prevention of clots in tubes and filters during transfusion of stored blood. On the apparatus used by most hospitals is a long glass inlet tube; to this two clove-hitch knots are tied with linen thread, one $\frac{1}{2}$ an inch from the free edge of the tube, and the other 5 inches from the first. Between these knots is wrapped a 10-inch length of 1-inch ribbon gauze, in a clockwise spiral. The gauze is then secured by winding the long end of one of the knots in an anti-clockwise spiral until it reaches the other knot, to which it is tied. The apparatus is then autoclaved in the usual manner. When a transfusion is to be given, the blood is left unmixed, and the cork holding the air-inlet and blood-delivery tubes is placed loosely into the neck of the bottle. The air-inlet tube pierces the clot lying on the surface of the corpuscles. The clot is caught on the gauze, and takes up the position of a half-closed umbrella. Before finally fixing the cork the blood is stirred gently with the air-inlet tube. This brings the rest of the clot into contact with the gauze to which it adheres. The blood is then mixed thoroughly by inverting the bottle several times. During this procedure the rubber 'policeman' should still be on the atmospheric end of the air-inlet tube, and the delivery tubes should be compressed to prevent loss of blood. The bottle is then hung on its stand. During the mixing of the blood, and throughout the transfusion, the clot remains firmly adherent to the gauze arrester, and does not in any way interfere with the flow of blood.

A device for warming refrigerated blood.—T. H. Seldon describes and illustrates a metal hot-water container for warming cold refrigerated blood before its transfusion into the recipient's circulation. It consists of two separate metal containers hinged together. Each container measures 8 × 5 × 1 inch and holds approximately one pint (500 cubic centimetres) of water. On the two adjacent surfaces a groove runs longitudinally in which the tubing of the intra-venous set is placed. The temperature of the water in the containers is 104° F. (40° C.), and sufficient heat is conducted through the metal and the rubber tubing to make an appreciable difference in the temperature of the cold blood. Though cold refrigerated blood can be given without significantly lowering the bodily temperature or any bad effects, many prefer to give blood warmer than 35° to 45° F. (2° to 7° C.).

Concentrated suspension of red cells for anaemia

D. H. C. MacQuaide and P. L. Mollison describe a method for the preparation and use of a concentrated suspension of red blood-cells in certain cases of anaemia. Advantages of this red-cell suspension over whole stored blood are that less than half the usual volume of fluid will produce the same rise in haemoglobin; the plasma of stored whole blood can be saved for use in the treatment of shock; reactions are fewer; and the danger of transfusing potentially incompatible agglutinins when using group O (IV) blood is greatly lessened. In a series of 61 cases in which the suspension was given, the incidence of rigors was 6.5 per cent; in a similar series of transfusions with whole stored blood the incidence was 22 per cent.

Soluble protein and blood volume

G. A. Harrison and L. E. R. Picken state that, in cases of haemorrhage or circulatory shock,

the lasting restoration of the blood volume to its normal value by transfusion depends on the replacement of dissolved protein lost from the circulation as a result of injury. Since equal volumes of serum, citrated plasma, citrated whole blood, and defibrinated whole blood contain different amounts of dissolved protein, the volume to be transfused in any particular case will depend on the type chosen. The maximal volumes which can be safely given are: serum 3.4, citrated plasma 5.1, citrated whole blood 8, and defibrinated whole blood 6.6 bottles.

Plasma as a substitute for whole blood

As blood cannot usefully be stored longer than a few weeks, G. A. H. Buttle, A. Kekwick, and A. Schweitzer investigated experimentally the value of various substitutes for use in the treatment of acute haemorrhage. It was found that, in the cat, plasma was the only substitute which gave results approximate to those obtained with whole blood. The other substitute solutions tested, were placed in the following descending order of value: serum, haemoglobin-Ringer, gum saline, red blood-cells in crystalloid solution, isotonic saline, and isotonic glucose.

Whole blood in gastro-intestinal haemorrhage

D. A. K. Black and A. F. Smith found that, in 9 patients with severe haemorrhage from the stomach or duodenum, plasma compared unfavourably with whole blood in its effects on the blood volume and haemoglobin concentration. The degree of azotaemia was not lowered to the same extent as with whole blood, and the general condition of the patient was adversely affected. The ill effects of plasma in such cases may be due to forced dilution of the blood in excess of the limits within which blood dilution is favourable to recovery from haemorrhage. Generally plasma is contra-indicated when the haemoglobin is less than 50 per cent.

Sulphanilamide as a preservative for blood

R. F. Hunwicke confirms Novak's observation that sulphanilamide in comparatively low concentrations exerts a preservative effect on blood stored at refrigerator temperatures. He found that the drug is an effective preservative in concentrations of 1 in 1,000 to 1 in 5,000 for blood stored in the refrigerator at 2° C.

Storage of blood plasma

M. M. Strumia and J. J. McGraw, discussing the storage of blood plasma, maintain that storage in the liquid state should be discouraged, because of the opportunity for bacterial growth and continuous deterioration of many essential elements and the precipitation of fibrinogen. The difficulties are completely eliminated by collection of blood, separation and pooling of plasma by a rapid closed method, followed by immediate freezing and preservation in the frozen state. This method is simple and economical, and provides optimal preservation for such labile elements as prothrombin complement and fibrinogen.

Preparation of serum from stored blood

J. W. Clegg and J. H. Dible describe a method of preparing serum from stored blood with the advantages that the serum is sterile, of a satisfactorily high protein content, and can be given to patients irrespective of their blood groups. The process utilizes blood which has been in the bank too long to be used for whole blood transfusion, thus effecting a big economy. Blood is taken in the usual way from the donor and stored in an ice-chest for 7-10 days, during which time it is available for transfusion. Then, if unused, the plasma is converted into serum. The supernatant plasma-saline-citrate mixture is removed by suction through a closed circuit, the whole process taking place in a manipulation chamber. The plasma is then pooled in Winchester bottles. The fibrin is precipitated by the addition of calcium chloride, 20 cubic centimetres of an 8 per cent solution of calcium chloride per litre of plasma being used. If the mixed calcium and plasma is allowed to stand, a very large clot is formed which retains most of the serum. If, however, the plasma is shaken while the fibrin is being formed, there results a small firm fibrin clot with very little retained serum. The shaking is done in the Winchester bottle, in which some glass beads have been placed, and the stopper of which has been firmly secured with adhesive tape. The bottle is then placed on a mechanical shaker, and shaken rapidly; a firm clot forms and the serum is then poured through a muslin-lined funnel into the reservoir of the filter. For filtration the authors use a 20 centimetre two-plate 'Pilot'-type Seitz filter. A Ford S.B. pad is used and has proved to be an efficient bacterial filter. The filtered serum is led through rubber tubing to a five-litre flask. The M.R.C. bottle adapted for bleeding, with a negative pressure, is used.

Methods of concentration and drying of plasma

F. X. Aylward, B. R. S. Mainwaring, and J. F. Wilkinson describe two methods for the concentration and drying of plasma, namely spray distillation *in vacuo*, and adopting the principle of evaporation through cellophane tubes under sterile conditions, and subsequent low-temperature drying of the concentrate. These methods enable large amounts of plasma to be concentrated and dried without undue cost. Serum may also be concentrated or dried by those methods, and may prove to be more satisfactory than plasma.

Reactions After Transfusion

Stored human blood

E. L. DeGowin and R. C. Hardin, investigating the reactions after blood transfusion, found that the incidence of all types of reactions was no higher from the transfusion of preserved blood than from that of fresh blood, provided that proper care was taken in its storage and handling. The limits of storage time were arbitrarily placed at 10 days for citrated blood and

30 days for a dextrose-citrate mixture. Variations in the age of the blood used did not give any corresponding variation in the incidence of reactions. There were no types of reaction from the use of preserved blood which are not recognized as complications from transfusion of fresh blood. The authors consider that the presence of pyrogens in fluids or apparatus is probably a cause of many of the febrile reactions with blood transfusion.

Allergy induced by anti-haemorrhagic substances

K. P. A. Taylor reports a condition characterized by extreme refractoriness to blood transfusion and believed to be caused by allergy induced by anti-haemorrhagic substances. Sensitization after the use of moccasin venom has been reported. Allergy to liver therapy has also been observed. To obviate disturbances, patients undergoing treatment with biological anti-haemorrhagic substances should be frequently cross-matched with donors already determined as suitable subjects for transfusion.

Renal insufficiency

W. B. Daniels, B. W. Leonard, and S. Holtzman report 13 cases of renal insufficiency as a result of transfusion of blood; of these patients 6 recovered and 7 died. An immediate or delayed reaction occurred as a result of the transfusion, and this was followed by nausea, vomiting, haemoglobinuria, jaundice, oliguria, stupor, and uraemia. Leucocytosis, azotaemia, and acidosis were present in all cases examined. Five necropsies were carried out; of these 4 showed that the kidneys were large, swollen, and congested, and microscopical examination showed interstitial oedema, leucocytic infiltration, dilation of the tubules, and degenerative changes of the tubular epithelium. The remaining case showed central focal necrosis.

Survival of stored blood after transfusion

M. Maizels and J. H. Paterson found that stored blood survives for considerable periods after transfusion. Red cells stored for less than a week show about 70 per cent survival 24 days after transfusion. If storage is between 7 and 14 days, more than half the transfused red cells are still present in the recipient's circulation 14 days after transfusion. During storage normal cells lose potassium and take up a great excess of sodium. Within 24 hours of transfusion the chemistry of stored cells is restored to normal.

P. L. Mollison and I. M. Young gave 26 transfusions of stored blood to 20 patients and observed quantitatively the survival of the donor's cells by differential agglutination. In 4 cases two transfusions of blood stored for different periods were given simultaneously to the same patient. The fate of the cells of each transfusion was followed separately by a method employing the sera both of the ABO and MN systems. In this way a direct comparison of the survival of stored blood and fresh blood was made. It was found that a high proportion of the erythrocytes of stored blood survive transfusion, and that the total time of survival is little less than that of fresh blood. These observations suggest that the present method of storage employed at the London blood-supply depots is good, and that little more than the normal ageing process occurs, at least in blood stored for 18 days or less.

S. R. M. Bushby, A. Kekwick, and H. L. Marriott investigating the survival of stored red cells after transfusion, found that, when blood is collected into a 3 per cent solution of sodium citrate in the proportion of 100 cubic centimetres of citrate to 100 cubic centimetres of blood and stored at 4° to 6° C., the following procedures prolong the period of preservation of the red cells, as judged by a quantitative fragility test; adjustment of pH to 5 (of no practical value), dilution, and addition of glucose.

The fate of extra-corporeal circulating haemoglobin

N. H. Fairley reports the results of his further observations on the injection of haemoglobin and the subsequent quantitative estimation of the resulting haemoglobinaemia, as well as serial Van den Bergh and Schumm's (haematin) tests. Injections of haemoglobin were made into 3 male convalescents; 2 patients who underwent incompatible blood transfusions were also investigated, and intravenous injections of alkaline haematin were made into man and monkeys. After the intravenous injection of 14 to 25.4 grammes of human haemoglobin in man a positive Schumm reaction was invariably demonstrated in the plasma within 4 to 10 hours, and persisted for 24 hours or longer. A transient increase in bilirubin was also noted in the plasma of 2 out of the 3 patients receiving the injections. Although methaemalbumin was not found spectroscopically after injection of haemoglobin in these amounts, it was present in the plasma of the 2 patients who by mistake received incompatible blood containing approximately 45 and 90 grammes of haemoglobin respectively. In incompatible transfusion and other intravascular haemolyses in man, methaemalbumin and not methaemoglobin is found in the plasma; a mixture of the two pigments has never been recorded *in vivo* though they do occur together *in vitro* when a human plasma-haemoglobin mixture is incubated at 37° C. Extra-corporeal circulating haemoglobin may be (1) excreted by the kidneys, (2) absorbed by the reticulo-endothelial cells with the production of bilirubin and haemosiderin, and (3) katabolized in the circulation with the production of methaemalbumin. It is suggested that haemoglobin disintegrating in the circulation is first split into globin and reduced haematin (ferrous); the latter pigment is immediately oxidized to haematin (ferric) which in man combines with serum albumin to form methaemalbumin.

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BOILS AND CARBUNCLES

See also B.E.M.P., Vol. II, p. 547; Cumulative Supplement, Key Nos. 173 and 174; and Surveys and Abstracts 1940, p. 223.

Treatment

Suction

W. I. de C. Wheeler recommends suction for the treatment of boils and carbuncles. The type of case which responds best is that with wide-spread induration, toxæmia, and pyrexia. A Bier's cupping-glass is placed over the involved area and connected by pressure tubing to an electric suction apparatus, regulated so that the glass is held securely in position without pain. The strength of the suction is gradually increased until thick pus and blood well slowly into the glass. The process is continued for about 5 minutes, and repeated daily for a few days. After each sitting the patient usually admits considerable relief. The slough finally appears in the glass. A breast-pump forms a substitute for the cupping-glass, but causes more pain.

Sulphathiazole

G. Melton employed sulphathiazole in 50 cases of staphylococcal infection, mostly of the severe type. He found that it was of value when given early and in adequate doses, and that rapid improvement attributable to the drug occurred in 5 out of 13 cases. Many carbuncles ceased to extend after the drug was begun, and the period of pyrexia appeared to be shortened. The drug was of value, after surgical drainage, in clearing up toxæmia and hastening the subsidence of the local lesion.

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Wheeler, W. I. de C. (1940) *Lancet*, **2**, 683.

BONE DISEASES

See also B.E.M.P., Vol. II, p. 553; and Surveys and Abstracts 1939, p. 253; 1940, p. 224.

Congenital Bone Dystrophies, Generalized

Osteosclerosis fragilis generalisata (marble bones)

Clinical picture.—B. Vidgoff and G. J. Bracher report a case of osteopetrosis in a woman of 30, who showed the usual symptoms of the disease—encroachment of the bones of the skeleton on surrounding organs. The diagnosis was first suggested because of the presence of optic atrophy, anaemia, and the history of multiple fractures. X-rays showed the typical dense condition of the bones. The case was particularly interesting from the standpoint of the lack of familial incidence, the absence of consanguinity of the parents, the response of the blood condition to iron therapy, and the demonstration of changes in the optic foramina resulting in optic atrophy.

Idiopathic fragilitas ossium

Osteopathia condensans disseminata.—L. D. Baker and H. A. Jones report a case of osteopathia condensans disseminata (osteopoikilosis or 'spotted bones') in a boy of 8 years of age. The condition is congenital and the aetiology is obscure. X-ray examination shows spotted areas of increased density in the spongiosa, and streaks of condensation along the shafts. In the case reported both these types of lesion were present throughout the pelvic bones, the femora, the pubes, the right patella, the tarsal and metatarsal bones, and phalanges of the feet. There was also a disturbance in growth of one of the epiphyses, as well as numerous tendon contractures and deformity.

Pseudo-fractures.—J. A. L. McCullough reviews the condition of pseudo-fracture of bone, called by Looser 'areas of reconstruction', and commonly known as Looser's zones, which occur in a number of morbid skeletal states which are little or not at all related to each other, and may occur in otherwise apparently healthy bones that have been exposed to unusual strain. It has recently been suggested that the defect in the vertebral arch leading to spondylo-

bone neoplasms, such as benign osteochondromas and giant-cell tumours, produce little phosphatase; some osteogenic sarcomas produce little phosphatase, whereas others produce abundant phosphatase which does not readily enter the circulation; and some osteogenic sarcomas produce phosphatase which enters the circulation and can be measured in the serum. The phosphate-producing mechanism of most of these tumours is inactivated by radiation therapy when the tissue dose equals or exceeds 4,000 roentgens. Smaller doses cause only irregular or incomplete inactivation. Changes in the phosphatase content afford a prompt indication of the effect of radiation therapy.

Malignant

Solitary myeloma.—L. W. Paul and E. A. Pohle report on 4 new cases of solitary myeloma of bone, and review 45 cases (males 35, females 10) with an average age of 48 years. Solitary myeloma shows varying degrees of malignancy; some are much like giant-celled tumours. Two main groups have been described: (1) 'Solitary' only until generalization has taken place; this group illustrates the suggestion that there is not any essential difference between solitary and multiple myeloma; and (2) rare tumours running a course of 4 to 10 years. It would appear that 'solitary myeloma' is not identical with osteoclastoma (non-malignant giant-celled tumour, 'myeloid sarcoma').

Multiple myeloma.—L. C. Kinney reports 4 cases and discusses the subject of multiple myeloma of bone. The condition is regarded as a malignant osteolytic tumour arising from cells in the red bone marrow. It has been suggested that it may be a sequel of 'solitary' myeloma of bone (see above). The onset is not marked by characteristic symptoms, but Bence Jones's protein may appear in the urine, which often shows evidence of renal damage.

Osteoporosis

Intrinsic causes

Treatment of post-traumatic osteoporosis.—L. G. Herrmann and J. A. Caldwell state that post-traumatic osteoporosis is a definite morbid entity with characteristic X-ray changes in the three main stages of its evolution. If left untreated it may result in ankylosis of one or more of the joints in the region of the trophic disturbance in the short bones. Operations on the sympathetic system provide a rational and effective method of treatment. If operation is performed during the active phases of the disease, it responds quickly and the undesirable sequelae are prevented. Periarterial sympathectomy is generally sufficient for cases of post-traumatic osteoporosis limited to the distal part of the extremities.

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Kinney, L. C. (1940) *Radiology*, **35**, 667.

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Siegel, M. (1941) *Canad. med. Ass. J.*, **44**, 482.

Vidgoff, B., and Bracher, G. J. (1940) *Amer. J. Roentgenol.*, **44**, 197.

Woodard, Helen Q., and Higinbotham, N. L. (1941) *J. Amer. med. Ass.*, **116**, 1621.

BOTULISM

See also B.E.M.P., Vol. II, p. 589.

Treatment

Antitoxin

Importance of early administration.—In a review of the treatment of infections by methods other than chemotherapy, W. Thalhimer refers to the relatively uncommon occurrence of botulism in North America, and quotes the following figures from L. Velikanov and M. K. Kolesnikova: among 227 cases, 146 patients received and 81 did not receive serum, and served as controls; of the 81 controls 76, or 93 per cent, died; whereas only 26 or 18 per cent of the 146 patients succumbed. Large quantities of serum were given, each dose being from 60 to 100 cubic centimetres; some of the most severe cases received repeated doses at short intervals, a few as much as 600 to 700 cubic centimetres. In several apparently hopeless cases serum was given intravenously, and twice intrathecally in doses of 10 to 20 cubic centimetres, with astonishing recoveries. The best results were obtained when the treatment was given early in the course of the disease.

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BRAIN ABSCESS

See also B.E.M.P., Vol. II, p. 597; and Surveys and Abstracts 1939, p. 254.

Aetiology

Fungous infection

G. C. Anderson reports 4 cases of fungous infection of the brain in each of which the

condition was due to a different cause, namely coccidiosis, saccharomycosis, actinomycosis, and infection with a mycelium-producing organism. In 2 cases the lesions were abscesses of the brain, and in 2 encephalo-meningitis. In all 4 cases the diagnosis was verified by microscopic examination, and in 3 it was confirmed by necropsy. The pre-operative diagnosis in 2 cases was tumour of the brain. All 4 patients died.

Clinical Picture

In relation to congenital heart disease

I. S. Wechsler and A. Kaplan report 2 cases of cerebral abscess (paradoxical) and collected 12 previously published cases. In 10 of the 14 cases the abscess was on the right side, a possible explanation of which is suggested in the right-sided position of the aorta. The cerebral or cerebellar abscess, which occurred in 1 of the 14 cases, is usually single and runs a rapid course. In 3 only of the 14 cases was the condition recognized during life and therefore operated upon. As a rule embolism or thrombosis has been diagnosed and the rapid progress of the abscess in some degree justifies this. In doubtful cases pneumo-encephalography may be useful.

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BRAIN: REGIONAL DIAGNOSIS

See also B.E.M.P., Vol. II, p. 609; Cumulative Supplement, Key No. 188; and Surveys and Abstracts 1939, pp. 94 and 255; 1940, pp. 64, 71, and 228.

Symptom-Complexes Associated with Lesions of the Frontal Lobe (Pre-Rolandic Area)

Clinical picture

Agenesis of corpus callosum.—L. N. Goldensohn, E. R. Clardy, and Kate Levine report a case of agenesis of the corpus callosum in a girl aged 12. The chief clinical manifestations were overactivity, distractibility, temper tantrums, sexual preoccupation, inability to attend school, wetting, and occasional soiling. Physical examination showed several stigmata of degeneration and endocrine disorder. Neurological findings indicated organic involvement of the central nervous system. Electro-encephalographic studies indicated an absence of synchronism between the electrical activity of the right and left cerebral hemispheres. Pneumo-encephalograms revealed an absence of the posterior portions of the corpus callosum.

Symptom-Complexes Associated with Lesions of Optic Chiasma and Pituitary

Fractured skull and injury to posterior pituitary

Gastric changes.—K. Simpson records and illustrates the case of a labourer, aged 31, who died 44 hours after having a fractured base which involved the pituitary fossa, the stalk of the pituitary, and the region of the tuber immediately over the gland. The stomach showed a haemorrhagic condition strictly confined to the area of the gastric mucosa containing oxyntic cells; the chief change was the presence of capillary haemorrhage causing swelling of the interstitial tissues. Further, the oxyntic cells showed an unusual finely granular character. This appears to be the first human case of the similarly localized gastric lesion produced experimentally by the injection of posterior pituitary substance (E. C. Dodds, P. L. Noble, and E. R. Smith). Dodds and Smith subsequently showed the importance of acid reaction for this phenomenon, and it may be that the effect of the acid is merely to lower the threshold of another gastrototoxic substance.

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BRAIN TUMOURS

See also B.E.M.P., Vol. II, p. 619; and Surveys and Abstracts 1939, pp. 94 and 257; 1940, p. 229.

Pathological Classification

Non-malignant tumours

Acoustic neurofibroma.—G. S. Baker, A. W. Adson, and J. W. Kernohan record a case in a man, aged 45 years, of an acoustic neurofibroma of the dumb-bell type of the left 8th cranial nerve associated with an independent atypical astrocytoma of the vermis and left lobe of the cerebellum. Clinically the case showed complete left 8th nerve deafness, complete left facial paralysis, loss of taste sensation on the left side, an ataxic gait, and bilateral papilloedema. The diagnosis was a tumour in the left cerebello-pontine angle. At operation the left acoustic tumour was easily exposed and removed. The 4th ventricle and the aqueduct were not explored. Death occurred on the third post-operative day from pulmonary haemorrhage and early broncho-pneumonia. At necropsy there was a nodular rounded gelatinous tumour partly overlying the middle third of the petrous portion of the temporal bone in the left middle cranial fossa. This growth contained numerous smooth-walled cysts. It is difficult to explain the presence of the characteristic perineural fibroblastoma in the middle cranial fossa; there was a direct communication between the tumour in the cerebello-pontine angle and that in the middle fossa, as well as histological identity of the two neoplasms; it is not

clear why part of the tumour should extend through the hardest bone in the body instead of passing in its entirety into the posterior fossa, which is the route followed by practically all acoustic tumours.

Malignant tumours and non-malignant tumours

Stromal tumours of the choroid plexus.—According to A. F. Liber and J. R. Lisa, growths in the stroma of the choroid plexus include true neoplasms, nodular hyperplasia, simple cysts, concretions, and xanthomas. The most common neoplasm is the meningioma, which occurs almost exclusively in the lateral ventricles. Less frequent tumours are lipomas, sarcomas, angiomas, chondromas, teratomas, and doubtful cases of myxomas. In 3 cases of bilateral nodular hyperplasia in hydrocephalic infants the nodules were situated at the tip of a long stalk attached to the dorsum of the glomus of the choroid plexus. Xanthoma is rare. All stromatogenous growths and deposits occur in the glomus.

Clinical Picture

Cyst of the cavum vergae

W. Leslie reports a case in a man, born in 1896, of a cyst under the corpus callosum which was very thin, soft, and yellow in colour. This was associated with wide separation of the veins of Galen, a thin membrane resembling omentum, defects in the septum pellucidum and, from pre-operative encephalography, enormous dilatation of both cerebral lateral ventricles, and a diagnosis of an expanding lesion in the superior and posterior parts of the 3rd ventricle which was also greatly dilated. The contents of the cyst were clear. The operation took place in 1937, and since then there had not been any signs of increased intracranial pressure. Such cysts of the cavum vergae are very rare. In this instance symptoms—attacks of splitting headaches mainly at night and lasting 15 minutes—began in 1922, and when bilateral choked disks and greatly increased pressure of the cerebrospinal fluid were found, a left sub-temporal decompression was performed with great relief for 8 years. In 1930 the case was regarded as neurasthenia; in 1932 chronic arachnoiditis was suggested as the diagnosis. The author points out that tumours and cysts form a surprisingly large proportion of those cases in which a diagnosis of functional disorder has been based on a complaint of chronic or recurrent headache.

Special Methods of Examination

Ventriculography and encephalography

Diagnosis of cerebral tumour.—In their report on the altered behaviour of a prominent and much respected clergyman, aged 61 years, in whom the diagnosis between a focal lesion and cerebral arteriosclerosis with degeneration remained open, H. W. Woltman and W. McK. Craig balance the limitations and the value of electro-encephalography. Though it cannot be regarded as certain always to indicate the nature or the exact site of the lesion, particularly in those deeply situated, it is of value in cerebral localization, and in this case cleared the way for further investigation by encephalography and ventriculography which established the diagnosis of a large lesion in the right frontal lobe. A soft encapsuled meningioma was removed. Four months later the clergyman was normal.

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BRAIN: VASCULAR DISORDERS

See also B.E.M.P., Vol. II, p. 641; and Cumulative Supplement, Key No. 190.

Clinical Picture

Encephalopathy

As a result of sulphamethylthiazole therapy E. Roseman and C. D. Aring report a case of encephalopathy associated with the use of this sulphonamide. The chief lesions were focal perivascular haemorrhages in the grey matter of the cerebral hemispheres and the nuclear structures of the brain stem. There were focal perivascular areas of necrosis, apparently simultaneous diapedic haemorrhages, and profound alterations in the small blood vessels, chiefly of the endothelium; these often occluded the vessels. There was also severe anoxic neuronal damage.

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BREAST DISEASES

See also B.E.M.P., Vol. II, p. 657; Cumulative Supplement, Key Nos. 191–197; and Surveys and Abstracts 1939, pp. 35, 109, and 260; 1940, pp. 21 and 230.

Inflammations and their Treatment

Chronic mastitis

Testosterone inunction.—A. W. Spence found that the inunction of the breast with an ointment containing testosterone or testosterone propionate, rubbing in the equivalent of 3–10 milligrams of active substance daily, relieved mammary pain in 6 out of 8 cases of chronic mastitis. In the other 2 cases the relief could not be properly assessed. The treatment has the

following advantages over the use of intramuscular injections: it can be carried out by the patient; since comparatively small doses are effective, it is cheaper; there is no risk of producing such changes as increased growth of hair on the face, suppression of the menses, or hypertrophy of the clitoris; and it may be more effective.

Tumours and their Treatment

Malignant tumours

Treatment by irradiation.—E. P. Halley and P. J. Melnick recommend pre-operative irradiation of carcinoma of the breast for at least 4 or 5 weeks in order to reduce to a minimum the viable tumour cells. About 4 weeks after the end of irradiation the carcinoma begins to proliferate again from the surviving tumour cells, which remain in at least 90 per cent of irradiated mammary carcinomas. It is therefore important to operate early before the tumour resumes its growth. Amputation should not be delayed for 2 or 3 months as is usually recommended, but should be performed in from 2 to 4 weeks from the end of irradiation.

R. W. Teahan states that the advantages of interstitial radium irradiation in the treatment of mammary cancer are as follows: the breast, or a portion of it, may be saved; the risk is probably less than that of radical breast amputation; in some inoperable cases the disease may be destroyed; if necessary, the treatment may be repeated. Disadvantages are that it is not possible to implant bulky breasts and axillae so that anything like homogeneous irradiation is obtained; the length of stay in hospital and the period of convalescence are longer than with operation, irradiation fibrosis often limits arm movement; a closer follow-up to detect recurrences is necessary, and the retraction of the breast and the telangiectasis may be more disfiguring than an operation scar.

X-ray therapy.—S. G. Schenck states that, in stages 1 and 2 of breast cancer, radical surgery is indicated at from 6 to 8 weeks after a preliminary course of X-irradiation, and that a further course of irradiation should be given from 4 to 6 weeks after operation. The author considers that X-ray sterilization of the ovaries tends to improve the final results, and is advisable at least in all patients who are still menstruating. Patients in stage 3 should receive as thorough a course of X-rays as their condition permits, followed by conservative surgery or radium therapy, as the case indicates.

Additional physical sign.—C. E. Rees describes an additional physical sign of malignant tumours of the breast. In cases of a deep-seated tumour, fixation to the pectoralis major muscle occurs. This fixation, the detection of which is not always easy, can be demonstrated as follows: the patient, in the horizontal position, is requested to bring the arm on the affected side to a right angle and, with the examiner standing in the plane of the axilla on that side, exerts pressure with the arm against the examiner. This actively tenses the pectoralis major muscle so that, if the growth is attached to the pectoralis fascia, it will immediately become fixed and immobile.

Pathology of mucinous carcinoma.—O. Saphir states that mucinous carcinomas of the breast are not a single entity, but apparently consist of various forms of tumours of the breast. The true mucinous carcinoma consists of duct or cystic structures filled with mucinous material in which groups of, or isolated, tumour cells may still be recognizable. The duct carcinoma with mucinous features is the most frequent form. Areas similar to those seen in true mucinous carcinoma are intermingled with duct carcinomatous structures. The signet-ring cell mucinous carcinoma is characterized histologically by well-preserved mucin-secreting cells with basophilic or clear cytoplasm and crescent-shaped, compressed nuclei at the base of the cells. This tumour is very malignant. The fourth variety may be called the intracystic papilloma with mucinous features. It is relatively rare, and non-malignant.

Other Breast Conditions

Nipple discharge

Warning of disease.—P. R. Hinchey reports 67 cases of nipple discharge, 35 of which showed blood. Carcinoma, chronic cystic mastitis, and duct papilloma were responsible for about 75 per cent of the cases. The two latter conditions must be regarded as pre-cancerous. Twelve of 24 women with cancer had a non-sanguineous discharge. In 11 women the discharge was the first warning of any disease. In 4 women there was not any palpable mass in the breast at the time of their first examination.

H. K. Gray and G. A. Wood, in an analysis of 227 cases of papilloma of the breast, insist on the importance of any discharge from the nipple. In 48 per cent of the patients with malignant papillomas no tumour was demonstrable. In 60 per cent of all patients with malignant papillomas and with discharge from the nipple no tumour was palpable. All cases with discharge from the nipple should therefore receive most serious consideration, and in most cases operation should be performed.

Gray, H. K., and Wood, G. A. (1941) *Arch. Surg., Chicago*, **42**, 203.

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BRONCHITIS AND BRONCHO-PNEUMONIA

See also B.E.M.P., Vol. II, p. 696; Cumulative Supplement, Key Nos. 202-207; Surveys and Abstracts 1939, p. 266; 1940, p. 234; and pp. 3 and 71 of this volume.

Broncho-Pneumonia*Aspiration type*

Oil aspiration (lipid) pneumonia.—D. G. Freiman, H. Engelberg, and W. H. Merrit carried out a clinico-pathological study of 47 cases of aspiration pneumonia, largely, if not all, in adults, from the Montefiore Hospital, New York, an institution for chronic disease. The average age at death of 41 cases in which a necropsy took place was 61.8 years. The history of this form of aspiration pneumonia, which is comparatively recent and is not widely known, is given in full; in 1925 G. F. Laughlen reported 3 cases in men, but it had been experimentally produced previously by A. Guieysse-Pellissier in 1920. It occurs in infants and in debilitated patients with dysphagia, but there is good evidence that oil introduced into the pharynx may reach the bronchi without exciting reflex inhibitions. The oil, and particularly liquid paraffin, may be taken orally as a laxative, introduced intranasally in children, or given intratracheally. Fats and oils of animal origin play an important part in the production of the condition in infants and young children, but much less in adults. Vegetable oils are seldom responsible, and it is especially pointed out that iodized poppy-seed oil and iodized sesame oil used in bronchoscopy are not irritating chemically and are seldom responsible for oil pneumonia. Cream and cod-liver oil have been incriminated only exceptionally. The authors in addition to their own 47 cases brought the number of reported adult cases, including a girl of 17, up to 57. The morbid changes induced by aspirated oil, a chronic condition, consists of grey or pinkish or yellowish grey nodules of consolidation. Microscopically there are two stages; the first, accumulation of phagocytes (lipophages) in the alveolar spaces where they take up droplets of oil, is characteristic; later fibrosis occurs, the lesions become greyish white, and the histological changes are less specific and resemble those in chronic interstitial pneumonia. Half the subjects are free from symptoms but the radiological and physical signs may suggest chronic interstitial pneumonia or bronchiectasis. Stress is laid on the value of radiological examination; the presence of oil in the sputum is also diagnostic. The condition may be complicated by attacks of broncho-pneumonia, or death be due to other infections.

Clinical picture and treatment

In group of young adults.—C. E. Lyght and L. R. Cole report on 300 consecutive cases of pneumonia among university students during eight academic years. The incidence of the disease corresponded roughly with university sessions. Nearly 50 per cent of the patients had had previous illness, the commonest being respiratory infection. The lung lesion was of mild (broncho-pneumonia) type, but there were 11 lobar cases. There were 11 deaths, a low percentage, but the highest single cause of death among the students. The disease could not be diagnosed in its early stages in 50 per cent of the cases. The most frequent symptoms were cough, muscular pains, headache, coryza, chest pain, feverishness, sore throat, chill, hyperaemia of nasal and pharyngeal mucosae, tender eyes, slight cyanosis, flushed face, profuse perspiration, râles only at later stage, and moist râles after resolution. The initial fever was not usually high, averaging 100°-103° F. Pulse and respiration rate were not excessive but all three rose later. Four patients had no fever, 24 had a definite crisis, and the rest recovered gradually. Physical examination cannot be as satisfactory as X-ray examination, which disclosed pneumonia when the former method failed. Laboratory observations showed a preponderance of streptococci and pneumococci in the sputum. Influenza was found in 4 cases and tuberculous infection in 2 cases. Infection usually involved the tonsils and pharynx. The urine was usually normal. The leucocyte count rose steeply during resolution and convalescence; this is considered a favourable sign. Two hundred and thirty-four patients had complications and 55 had none. The usual complications were pleurisy, middle ear infection, and fatal issue. The most complicated and the fatal cases appeared in years of lowest incidence, thus mortality varies with the incidence of specific types of infection and not with its general incidence. Treatment was not specific. Neither serum nor sulphanilamide were used much. Codeine and morphine were helpful. Forcing of fluids, mustard, hot packs, warm turpentine stupes, and enemata were used, the last with caution. Oxygen therapy was liberally applied to allay coughs, dyspnoea, and headache, always with favourable results.

Treatment

Sulphonamide compounds.—S. C. Wagoner and W. F. Hunting report on the use of sulphathiazole on 55 infants and children with pneumonia, and of sulphapyridine on another group of 54 infants and children. In both groups the level of the drug in the blood was kept at about 4 to 6 milligrams per 100 cubic centimetres. No great difference was observed between the two groups in relation to the time at which a significant fall of temperature occurred or the time at which there was clinical recovery. In 2 patients in the sulphathiazole group and in 8 in the sulphapyridine group there was an unsatisfactory response to treatment. Vomiting occurred in 18 patients treated with sulphathiazole and in 34 with sulphapyridine. The authors conclude that the two drugs are equally efficient in the treatment of pneumonia.

Sulphathiazole.—C. C. Fischer and H. A. Agerty compare the results of this treatment with sulphathiazole of 19 cases of lobar pneumonia and 20 cases of broncho-pneumonia in infants and children, with a series (13 lobar pneumonias and 28 broncho-pneumonias) treated during

the previous year with sulphapyridine. Most of the patients with both lobar pneumonia and broncho-pneumonia responded promptly to the drug. In comparison with the sulphapyridine series, it appears that there was a more rapid fall in temperature in the broncho-pneumonia cases treated with sulphathiazole. There were two fatalities in the sulphathiazole series; pneumococcal meningitis developed in one patient who did not respond to serum therapy or chemotherapy; the other patient was moribund on admission, and died 8 hours later. In the sulphapyridine series there was 1 death from a complication of streptococcal meningitis. Toxic symptoms and signs were not prominent. There appeared to be less nausea and vomiting than with sulphapyridine. There was no marked influence on the blood picture. The authors conclude that sulphathiazole compares favourably with sulphapyridine in the treatment of pneumonia in infants and children.

In children under one year of age.—A. M. Gill reports 11 cases of broncho-pneumonia in infants under 1 year of age in which the mortality rate is usually very high, even 90 per cent, but in this series was 36 per cent. This comparatively low rate is ascribed to the routine use of the oxygen tent and the administration of sulphapyridine. The dosage of the drug was 0.125 gramme 4-hourly up to the age of 3 months, and 0.2 gramme from 3 months to 1 year of age. The initial dose was double the maintenance dose. The oxygen tents employed used oxygen at the rate of 2.5 litres a minute, and the inside temperature was maintained at 70° to 74° C. Feeds were given 2-hourly, day and night, and half-strength saline freely was alternated with the feeds.

Chronic Bronchitis

Treatment

Ammonium salts as expectorants.—S. Alstead investigated the action of ammonium chloride and ammonium carbonate in chronic bronchitis. He found that doses of ammonium carbonate 6 times greater than the maximal official dose rarely caused nausea. There was not any evidence that either ammonium carbonate or ammonium chloride had any effect on expectoration in bronchitis. Although these drugs are not, as is generally supposed, contra-indicated in chronic bronchitis and bronchiectasis with profuse secretion of sputum, the results of this investigation do not justify the view that they are of any value in this disease.

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BURNS AND SCALDS

See also B.E.M.P., Vol. II, p. 719; Cumulative Supplement, Key No. 209; Surveys and Abstracts 1939, p. 267; 1940, pp. 10 and 236; and pp. 1, 11 and 38 of this volume.

Pathology

First degree burns

Histopathological changes in the liver.—L. J. Buis and F. W. Hartman, as a result of examination of 5 cases of death as a result of superficial burns, found the following histo-pathological changes in the liver: extensive degeneration of the parenchyma varying from true necrosis to congestion, vacuolization, and slight increase in peri-portal fibrous tissue. Similar hepatic changes were produced in experimental animals. Both the patients and the animals showed loss of plasma and haemo-concentration; accompanying the latter there was always the picture of acute passive congestion of the tissues, especially prominent in the liver. The authors believe that such engorgement of the sinusoids, coupled with stagnation of the circulation, was at least partly responsible for the degeneration of the liver cells, at the centre or throughout the lobule, as found in chronic passive engorgement. In congestion there is an inadequate oxygen supply to the liver cells, and metabolites tend to accumulate.

Clinical Picture

Encephalopathy

Neurological after-effects.—Neurological changes in the central nervous system due to severe burns have previously been demonstrated, and N. Roth reports an additional case of this occurrence. The patient, a girl aged 8 years, was admitted to hospital with severe burns covering 30 per cent of the body surface. After tannic acid and supporting treatment including intravenous fluid injections had been given, the patient had a high temperature and three rigors, but after 12 days she began to recover and was free from any mental abnormalities. After another 8 days the fever returned and the patient's condition became critical. After treatment, physical conditions improved, but neurological changes appeared; these included mental backwardness, inability to speak, irritability, lack of understanding, athetosis, and slight ankle clonus. Examination of the head revealed hydrocephalus and cortical atrophy. The electro-encephalogram was abnormal. The nature of the lesion and its delayed appearance

suggest that the after effects of burns are not due to locally produced toxins, but to the escape of plasma from the capillary walls into tissue spaces causing oedema of the organs.

Treatment

Symposium on war burns

Three essential factors.—C. P. G. Wakeley opened a combined discussion before the Sections of Surgery and of Therapeutics and Pharmacology of the Royal Society of Medicine, and pointed out that before the outbreak of war in 1939 the tannic acid treatment was considered to be completely satisfactory. War burns differ from those in peace-time; they are caused by gun-flash, bomb-flash, incendiary bombs, and petrol, and less often by chemicals or electricity due to broken cables and short circuits; in addition, the patients may not reach hospital for many hours or even days. War experience showed up the inadequacy of the tannic acid treatment, and accordingly many other forms of treatment were employed. First-aid treatment, which is all that can be satisfactorily carried out away from hospitals, consists in morphine to relieve pain, warmth, fluid by the mouth to counteract shock, and in severe shock, plasma transfusion. Morphine, which never kills a man who is in pain, should be given freely and repeated. (For local treatment see below.) Most war burns consist of a mixture of first, second, and third degrees, but some involve total loss of skin (third degree), and medical officers should distinguish between partial skin loss (second degree) and total skin loss. In treatment three essential factors must be considered. (1) Shock may be (a) *primary*, depending mainly on the extent rather than on the depth, and characterized by fall of blood pressure, feeble pulse, and cold clammy skin; the treatment is that described as first aid; (b) *secondary* shock occurs some hours later, is much more serious, 80 per cent of the total deaths from burns being thus caused, and as it is due to loss of plasma from the burnt surfaces and into the tissue spaces, plasma (not whole blood) transfusion is recommended. Intravenous normal saline or sterile water is contra-indicated. (2) Toxaemia, though its causation is open to discussion, is probably due to streptococcal infection; for cases with extensive burns and toxaemia the use of saline baths has proved very beneficial. (3) Sepsis is a serious problem, not yet finally solved; in first and second degree burns sepsis can be prevented if the new local coagulation treatment is employed immediately after the injury, and is followed by adequate cleansing and coagulation treatment on admission to hospital. Of the third degree burns 90 per cent become infected, usually by a haemolytic streptococcus.

Local treatment.—This describes the new coagulant method in place of the tannic acid treatment. The first-aid treatment must be simple, painless, and quickly applied. A jelly preparation contained in a tube is the best: there is no time or space in a battleship during action or in a tank or aeroplane for the use of a spray or surgical cleansing. A number of jellies are available, but Wakeley, having tried them all, prefers one of gentian violet with merthiolate (1 : 5,000); this can be applied to the burnt area without any cleansing, and should be liberal, for it is painless and even soothing. It seals off the burnt area and a crust forms which remains in place until the patient is admitted to hospital. The local treatment should not be given in the presence of shock, which should always be treated before any applications are adopted. Tannic acid should not be used on the hands or face; in the case of the fingers the unyielding tannic acid coagulum encasing the digits causes oedema which impairs the circulation, and terminal necrosis of the phalanges may follow.

Hospital treatment.—For shock, oxygen administered by the B.L.B. mask has prevented death. After this the patient is taken to a warm operating theatre and anaesthetized by gas and oxygen; the whole burnt area is thoroughly cleansed by saline, then dried by an electric hair-drier, and a watery solution of triple dye (2 per cent gentian violet, 1 per cent brilliant green, and 0.1 per cent neutral acriflavine) is sprayed on the surface; this is then dried, a second spraying and drying is carried out, and a supple tan adherent everywhere results. As a rule the tan becomes loosened about the eighth or ninth day and gradually falls off bit by bit, leaving a healed area. The administration of sulphanilamide in septic cases is discussed, but contra-indications are given, and it is regarded as seldom necessary. Chemical burns have not been much in evidence, but phosphorus from the back-flash of incendiary bombs has caused burns. Electrical burns have been not infrequent in the navy.

Complex systemic disturbances.—W. C. Wilson reviewed the complex systemic disturbances and their treatment. The relation between the immediate destruction of skin, blood vessels, and nerves by excessive heat and the production of shock, acute toxaemia, and sepsis was analysed. Attention has previously been mainly directed to the effects of injury to the minute blood vessels and capillaries; much less is known about the effects on the tissue cells, nerves, lymphatics, and blood circulating in the skin at the time of the injury. It is not improbable that damage to these structures may have important consequences; it has been assumed that painful impulses from many injured nerve terminations are responsible for the initial shock that sometimes appears very soon after the burn. Experience, however, shows that the common form of burn shock is the delayed or secondary, and it is not known if nerve impulses play any part in originating or perpetuating secondary shock; there is general agreement that the main factor is damage to the blood vessels and increased permeability, leading to concentration of the blood, but it is by no means certain that plasma loss is the only cause of secondary shock. In the next phase, toxaemia, of systemic disturbance, varies much in severity; the main features of a grave case are fever, anxiety, or stupor progressing to delirium or coma, vomiting, sometimes of blood, slight jaundice, albuminuria, and circulatory failure. The characteristic

morbid change is degeneration and necrosis of the liver cells, which, however, is probably never seen after infections, even of the most virulent kind, by the bacteria commonly present in burns. There are objections to the hypothesis of tissue autolysis, the most serious being that aseptic autolysis does not produce potent toxins. It is suggested that possibly autolysis is effective in the production of toxins only if accelerated and augmented by bacterial action. In sepsis the haemolytic streptococcus is often present, but Wilson has found *Staphylococcus aureus* in many infected areas. Fortunately secondary shock responds to treatment, and in the most severe cases a useful adjuvant is desoxycorticosterone acetate which rapidly corrects most of the blood changes. For local application the coagulation method is the most suitable, and he recommends a 10 per cent solution of silver nitrate, preceded and followed by the application of 1 per cent crystal violet. For areas which cannot be constantly exposed to the air, or for any reason cannot easily be kept dry, the following jelly preparation is useful: tragacanth 2 parts, glycerol 10 parts, powdered charcoal (B.D.H. activated) 15 parts, silver nitrate 0.5 part, and water to 100 parts.

Plasma.—L. J. Witts regards the dangerous period from shock as lasting for 24 to 48 hours; after this, death is unlikely to be due to shock, but may be caused by toxæmia or pneumonia. Plasma treatment should be begun as soon as possible; plasma drip may be maintained during the local treatment and for some hours longer, but intravenous fluid is not needed after the second day. The administration of plasma or serum brings about striking improvement: peripheral cyanosis disappears, the blood pressure rises, the pulse increases in volume, and patients are more able to take fluids by the mouth. Plasma is indicated when there are any signs of shock, such as pallor, collapsed veins, peripheral cyanosis, and fall of blood pressure. The earliest sign is a rise in haemoglobin, and patients with 10 per cent above their probable previous level, which in the young and healthy may be taken as 100 per cent, should receive plasma. Concentrated serum is much less effective than citrated plasma in producing haemodilution.

Function.—A. H. McIndoe, dealing with the functional aspect of burn therapy, finds that the evidence under war conditions is that the easily applied coagulation method so successful in the prevention of toxæmia has been carried too far, particularly in the coagulants which form a hard, inelastic crust. When the loss of skin is of the first and second degrees, the coagulation method gives excellent results, but when the loss of skin is of the third degree (full thickness) the coagulation method may, and usually does, fail, particularly as regards ultimate function. A description was given of the airman's burn; it has almost unvarying characteristics unlike any seen in civilian life. It is due to sudden exposure of unprotected parts of the body to intense dry heat or flame, as though the entire patient was thrust into a furnace for a few seconds and then withdrawn; it is rarely due to the burning of liquid petrol on local skin areas. The distribution is characteristic: both wrists and hands, especially the backs and fingers, the face in the 'helmet area', the neck between the chin and the collar, and the anterior surface of the thighs, if the trousers are thin. Coagulants containing a tannic preparation used at first-aid posts on burns of the face and hands have long been advocated; but the application is usually made hurriedly and inadequately over uncleaned surfaces. An alternative to coagulation treatment of burns of the face and hands is the use of saline packs and baths.

Envelope method.—J. Bunyan described the envelope method of treating burns. In addition to the general principles underlying the treatment of all kinds of wounds, that of burns demands the following conditions: (1) avoidance of aggravation of shock; (2) prevention of acute toxæmia from breaking down of damaged tissue; (3) primary disinfection and prevention of secondary infection; (4) control of the loss of body fluids and salts from burnt areas; and (5) stimulation of new formation of tissue without the production of scarring. The best method of meeting these requirements is by intermittent irrigation with weak solutions of electrolytic hypochlorites, which have the following properties: (a) selective action—the solution of dead tissue and the stimulation of healing tissue; (b) the breakdown products are salt and oxygen; (c) the great bactericidal powers in non-irritant concentrations; (d) stability and constant strength of stock solutions; and (e) relief of pain and desensitization. The treatment consists of (1) hosing-down the burnt area by a 5 per cent solution, which removes all surface contamination, much of the charred tissue, all the exudates, and most of the bacteria; (b) the application of the appropriate coated-silk envelope to the burnt limb or part for irrigation first, by sterile water at 100° F., and then by normal saline containing 5 per cent of electrolytic hypochlorite. The envelopes are made of a fine pure silk cloth coated with synthetic resins which are not affected by hypochlorites or boiling and render the silk watertight. The covered silk is transparent so that the process of healing can be observed. The use of the method was discussed in primary and secondary shock, disinfection, and prevention of secondary infection and of tissue toxæmia. The treatment can be applied quickly, easily, painlessly, and without complicated apparatus.

Powdered sulphonamides.—H. Gillies and L. Colebrook both are in favour of the local application of powdered sulphonamides to burns.

Plasma protein transfusion

According to R. Elman, the general manifestations of a severe burn are due largely to rapid and extensive loss of both tissue and, especially, plasma protein. Replacement of the latter by plasma transfusion is essential to maintain the circulation and to obviate the concentration of blood. The plasma loss is so great that 10 cubic centimetres of plasma or 20 cubic centi-

metres of whole blood per kilogram of body weight may have to be given or even repeated. As soon as nourishment by the mouth is possible, a high protein diet must be given. If blood is not available, a single injection of acacia may be used, but this is greatly inferior to plasma. The injection of large amounts of dextrose and saline solution alone in severe burns may prove to be, not only ineffective, but even harmful.

J. R. Elkington, W. A. Wolff, and W. E. Lee studied 5 cases of moderately severe burns, in the light of recent experimental and clinical observations. The results are in accordance with the view that the fluid imbalance is primarily due to an altered capillary permeability with a shift of fluid and protein into the tissues, rather than to an external loss. The restoration of plasma protein by means of plasma transfusion is a rational treatment for this fluid shift. Evidence is presented that the loss of plasma protein continues until the thirty-first to the fortieth hours. During this period excessive haemo-concentration may be prevented by small repeated plasma transfusions. Whether or not this period of healing is a general biological property of damaged capillaries could not be stated from the evidence at hand. After the fortieth hour, when the capillaries have regained their impermeability to protein, the deficit of plasma protein may be corrected, quantitatively, by a large plasma transfusion.

Plasma and serum transfusion

D. A. K. Black made clinical, haematological, and biochemical observations on 8 patients with burns and scalds; of these 7 were treated with plasma or serum transfusions. Before treatment the chief findings were as follows: increasing shock, with the typical symptoms; progressive haemo-concentration; a fall in the plasma volume, and consequently in the total amount of plasma protein, although the protein concentration was often quite high. There was evidence that amounts of plasma protein equivalent to one-quarter of the total plasma protein might be lost in a few hours; plasma chloride was high and plasma bicarbonate low, blood urea being normal; and serum sodium was low, with a slight rise in serum potassium. After the infusion of dilute plasma there was great clinical improvement, which was accompanied by a rise in plasma volume in those cases in which serial observations of blood volume were possible. The results with four times normal serum were much less favourable. One of the 3 patients treated died and the other 2 required an infusion of dilute plasma later.

Cod-liver oil and carron oil

W. Clayton, A. J. Howard, and D. Thomson found that healing of burns is promoted and regeneration of damaged tissue occurs more readily when burns are treated with carron oil or cod-liver oil than when they are treated with tannic acid. The scabs formed with tannic acid tended to be hard and somewhat brittle, whereas in all oil-treated cases they were soft and flexible.

Silver nitrate, tannic acid, and gentian violet

J. A. Ross and K. F. Hulbert employed silver nitrate, tannic acid, and gentian violet in 5 cases of extensive superficial burns with successful results. In spite of the various anaesthetic agents employed there was a noteworthy absence of sepsis and pulmonary complications. Before the application of the solution, thorough gentle cleansing is essential. The burnt areas are then painted with a 1 per cent aqueous solution of gentian violet, followed by a 10 per cent solution of silver nitrate and a 15 per cent solution of tannic acid alternately, dabbed on with gauze swabs. A firm coagulum forms almost immediately. The area is wrapped in sterile towels, and the patient returned to bed and placed under a cradle. The towels are then removed and radiant heat applied. Throughout the next 48 hours the 3 solutions are applied, in the above order, every 2 hours, by means of camel-hair brushes. Thereafter the solutions are applied 3 times a day for another 2 days, and once daily for a further 3 days. In cases of burnt limbs, these are kept at rest in suitable splints in the early stages, to prevent contractures.

Use of adrenal cortical extract in shock

Effect on plasma transfusions.—J. E. Rhoads, W. A. Wolff, and W. E. Lee describe the effects of adrenal cortical extract in the treatment of shock due to burns. The increase in plasma volume resulting from plasma transfusions is not sufficiently stable to compensate for the continuous loss, and capillary recovery is not complete before 40 hours have passed. Two groups of patients with burns were examined and given plasma transfusions until the hematocrit reading was kept below 55 and the plasma protein level above 6 grammes per cent. In addition adrenal cortical extract (5–10 cubic centimetres) was given intravenously every 6 hours to the first group. With one exception the patients showed a sharp rise of plasma volume before the thirtieth hour (and some before the eighteenth hour). The exception was a diseased and alcoholic patient. Patients of the second group did not show a rise in plasma volume before the thirty-sixth hour; furthermore, they required more plasma than the others. Cortical extract alone will not increase the plasma volume, but will only assist in the retention of plasma transfusions. It thus shortens the early 'danger' period after burns. A formula to determine the amount of transfusion needed by each patient is given.

Modern methods

General review.—R. Mowlem points out the dangers of tannic acid treatment for burns and outlines a safer and more effective method. Secondary shock should be treated by the restoration of the lost protein. Toxaemia is difficult to treat, but blood transfusions and a high carbohydrate diet are indicated. Damaged tissues may be removed by fomentations, saline packs or baths, hydrogen peroxide, or even by surgical means. The use of trypsin is under investiga-

tion. Powdered sulphonamide is recommended as an anti-infective agent and not tannic acid, because regeneration is delayed by the damaging action of the coagulum and the fixative action of its accompanying dyes and the resultant scar is of poor quality. In burns involving the whole thickness of the skin tannic acid may sometimes be used, except near orifices or across flexures; again, tannic acid harbours underlying infection, cannot be separated by desquamation, and delays skin grafts which must be applied as early as possible.

After the affected part has been subjected to frequent immersions in saline baths with intervening saline dressings, sulphonamide powder should be sprinkled on the wound daily. Pressure is maintained by wool wrung out in paraffin-flavine emulsion. The use of tannic acid for severe burns of the hand is condemned. It compresses the hand, prevents transudation, and fosters infection.

Glycerin-sulphonamide paste

J. M. Robson and A. B. Wallace describe a method of treatment to meet the three principles underlying the care of burns, namely (1) to save life, (2) to prevent infection, and (3) to obviate deformities, especially of the hands. This method consists of the application to the burnt areas of a water-soluble sulphonamide, albucid (*p*-aminobenzenesulphonacetamide), forming a neutral solution in glycerin. As glycerin alone is not suitable as a local application, the neutral solution is mixed with kaolin to form a paste (euglamide) to which is added a little cod-liver oil, in order to prevent the drying of the centre of the treated area, shown in preliminary observations. The paste exerts a soothing action, and allows early movements to be undertaken; this is important, for the immobilization of the parts associated with the use of coagulant agents tends to prevent subsequent restoration to normal functional activity. Twenty cases are tabulated, 15 of which had been treated by other methods, such as olive oil and tannic acid jelly. Success followed the use of albucid in burns of the hand (second and third degrees), the face and scalp (second and third degrees), the buttock (second and third degrees), the penis and scrotum (second degree), in burns septic after 24 hours of wet dressings, and in burns of the second degree when not extensive. A leading article in the same issue as that containing Robson and Wallace's article reviews the modern treatment of burns.

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Leading Article, *Brit. med. J.* (1941), **1**, 484.

CAISSON DISEASE

See also B.E.M.P., Vol. II, p. 730; Cumulative Supplement, Key Nos. 210–211; Surveys and Abstracts 1939, p. 270; 1940, p. 239; and p. 32 of this volume.

Clinical Picture

Helium-oxygen therapy

W. H. Requarth advocates helium-oxygen mixtures in aero-otitis media, a condition found among aviators and compressed-air workers. It is the result of blockage of the Eustachian tubes under changing atmospheric pressures. The most important disposing factor of blockage is, in the author's experience, infection of the upper respiratory tract, such as the common cold, sinusitis, or pharyngitis. The symptoms vary from slight impaired hearing with a sensation of pressure in the ear to decided auditory impairment, tinnitus, and severe auricular pain. The patient often expectorates bright-red blood, and occasionally there is haemorrhage from the external ear. The ear-drum is retracted and may show dusky red hyperaemia. In severe cases the middle ear is filled with a sero-sanguineous fluid, the drum is a dark bluish-red, and there is a middle-ear type of deafness. In some cases the fluid becomes infected, and typical suppurative otitis media ensues. The author found that a mixture of 80 parts of helium and 20 parts of oxygen, administered by means of a constant pressure apparatus, gave complete relief in 55 per cent, and moderate relief in 19 per cent of patients.

Requarth, W. H. (1941) *J. Amer. med. Ass.*, **116**, 1766.

CANCER

See also B.E.M.P., Vol. II, p. 737; Cumulative Supplement, Key No. 212; and Surveys and Abstracts 1939, pp. 28 and 270; 1940, p. 239.

Pathology and Aetiology

Carcinogenic action of oestrogenic substances

Oestradiol benzoate and stilboestrol.—C. W. Hooker, W. U. Gardner, and C. A. Pfeiffer report that a large interstitial-celled tumour of the testis, with metastases in the lumbar and renal lymphatic glands, appeared in a mouse of the A strain which received oestradiol benzoate for 264 days. In a second mouse a similar testicular tumour, which did not metastasize, and also in another mouse of the same strain receiving stilboestrol. The histological picture of the accessory organs of reproduction in both instances indicates that these tumours secreted androgenic material.

Composite factors of genesis of cancer

W. C. MacCarty, Sen., who has written much on the pathology of malignant disease since 1913, collected in 1919, 27 short summaries or definitions of just what cancer is, and now presents his conceptions of the genesis of cancer. Destruction of cells is the essential biological causal factor; alone it does not always cause cancer, but it is often followed by lipid or fatty degeneration, some of the products of which very probably alter cellular surface conditions and set up cellular hyperplasia. Wherever lipid degeneration occurs, its products or hydrocarbons must be either removed or continue their stimulating effect. The outstanding characteristic of cancer is the migration of cells, and writing nearly 30 years ago MacCarty pointed out that in the mammary acini specific or milk-producing cells are sometimes destroyed and that this process stimulates hypertrophy and hyperplasia of the reserve cells. Reaction in the surrounding tissues—lymphocytic infiltration, fibrosis, and hyalinization—interfere with food supply and so the hyperplastic cells might become migratory.

A similar reaction by aphids is noted, in which interference with food supply leads to the production of the migratory form, illustrating a basic biological phenomenon. The observations on breast tissue had been made in other tissues.

Sarcoma arising from a haematoma.—J. J. Eller and L. H. Kest report a case of sarcoma arising in an organized haematoma following a single trauma. The patient, a man aged 40, bumped his forehead against a beam, and a haematoma the size of a small marble appeared. It remained the same size for about 6 months when a practitioner made an unsuccessful attempt to aspirate the contents. The swelling gradually enlarged, and was excised; but 4 months later it recurred as a pea-sized nodule with some infiltration and fixation of the skin to the underlying tissues. Another wide excision was made. Histologically it was either a fibrosarcoma or an angiosarcoma of low-grade malignancy.

Effects of oestrogen and androgen on cancer tissue

Experimental investigation.—J. Heiman reports on the effects of oestrogen and androgen on spontaneous and transplanted mammary tumours in rats. Primary tumours were first removed and tumour fragments from these transplanted into the same or different animals of the same species. In most cases auto-transplants showed the same structure as the original tumour. The hetero-transplants varied in their reactions. Adenofibromas transplants took on the structure of the host's primary tumour, but fibromas remained fibromas whatever the structure of the primary tumour. A series of rats were given oestrogen (0.1–2.5 milligrams) and the transplants were repeated. Primary tumours were not affected, but hetero-transplants of adenofibromas on to a treated host became adenomas with considerable epithelial growth. Transplants of fibromas remained fibromas except on hosts with primary adenomas when they became slightly glandular. Epithelial transplants into fibromatous hosts became adenofibromas but gradually reverted to fibromas. Thus oestrogen appears to promote epithelial but not mesodermal growth. A second series of animals were given testosterone propionate (5–15 milligrams). Spontaneous tumours were unaffected. Adenofibromas transplants were inhibited, but later produced small fibromas. Fibromatous transplants were not affected. Thus the hormone appears to have an inhibitory action on epithelial growth, but not on mesodermal tissue. This fact has been used previously to reduce mortality and metastasis in rabbits with tumours. A third series were given androgen and oestrogen together in the ratio of 10 : 1. Spontaneous tumours were not affected. Transplants also grew, although the latent period of growth increased. Thus the action of oestrogens inhibits that of androgen and is predominant over the latter. Not in any case was carcinoma induced by oestrogen.

Diagnosis

By biochemical methods

D. L. Woodhouse points out that methods of biochemical analysis in the early diagnosis of cancer have not been proved to be adequate. The constituents found in the method of blood analysis could be attributed to secondary effects. The changes of surface tension, pH, sedimentation rate, and other forms of physico-chemical analysis are not specific to cancer, but the method of testing the reactions of tumour extracts and the use of hormones offer better possibilities. No specific cancer product which gives a specific reaction is known, cancer cells, according to one hypothesis, being normal cells with a special propensity for growth. The production of specific antibodies is doubtful, although animals have been known to acquire immunity to implanted tumours. Three biochemical tests were investigated as follows. (1) This had been previously used to demonstrate that normal serum and cancer serum speed up lipolysis—cancer serum to a lesser degree in certain instances. The inactive element of lipase (prolipase) was used in emulsified olive oil and the serum used as an activator.

The previous claims were not confirmed. (2) The vanadate flocculation method depends on the flocculation in a solution of sodium orthovanadate by different types of protein. Untreated serum protein, protein denaturalized by heat, and protein with the lipin removed were compared. The difference between the first and the second results (or 'heat effect') was taken to represent the patient's resistance to a process; between the first and third ('ether effect') to represent the extent of pathological change, the ratio between change to heat effect being the degree of malignancy. The diagnosis corresponded with clinical diagnosis in 74.8 per cent of the malignant and 74.4 per cent of the non-malignant cases tested. (3) The Fuchs test was based on the instigation of proteolysis by the reaction of normal serum protein and cancer serum (or cancer blood protein and normal serum) compared with a slower rate of proteolysis using normal protein with normal serum. The results agreed with clinical diagnosis in 94 per cent of the malignant cases tested and 90.3 per cent of the non-malignant cases. The author concludes that none of the methods is specific enough to be reliable, the Fuchs test being the best. It is, however, significant that the tumour produces active extracts at all.

Treatment

By gonad extracts

W. H. Lewis employed injections consisting of a mixture of the juices obtained by the maceration of fresh animal ovaries and testes (from cattle), in 28 cases of malignant disease. The serum obtained after centrifuging the juices was injected, generally upon alternate days, in doses of from 0.5 to 10 cubic centimetres. In all cases treated there was a modification of the malignant process, a recession or arrest of the growth, and relief of pain and bleeding, when present. The more recent areas of growth or extension appeared to be most readily affected. What may be termed the primary areas remained resistant, and in no instance did they clear up entirely. After cessation of treatment and recurrence of activity, all new growths seemed to progress more rapidly than usual. The author considers that the results obtained suggest that there exists in the ovary and testis a potent element which affects malignant growths.

Cobra venom

The successful use of cobra venom for the relief of pain due to cancer is reported by P. J. Hodes and R. S. Thorner. Out of 21 patients treated, 11 gave a good response; 6 received moderate relief, and 4 little or no relief. The venom was administered intramuscularly in small doses of 0.5 cubic centimetre of the commercial preparation and raised to 1 cubic centimetre on the second day, if no untoward reactions occurred. Momentary intensification of pain at first does not contra-indicate its further use. Complete relief from pain generally follows the fifth injection; the intervals between injections are then gradually lengthened. There have been few reactions, none so serious as to interrupt the injection. On the basis of animal experiments the venom should not be used for patients with severe renal, hepatic, or psychical diseases.

Local and general low-temperature treatment

A. J. Jones, J. Graham, and A. Mueller review this palliative treatment of inoperable and advanced cancer by the local (refrigeration) and general (hibernation) lowering of the body temperature. Local hypothermia was introduced by T. Fay and G. C. Henny (1938), and general hypothermia in 1939 by L. W. Smith and T. Fay, who described their clinical results as follows: (1) reduction of pain, (2) diminution of the size of the tumour, (3) general improvement in the patient's general condition, (4) retardation of metastases, and (5) degeneration of the tumour cells as shown by biopsy. Jones, Graham, and Mueller record their experience of both the local and the general applications of cold on 14 patients, most of whom had been treated by deep X-rays up to their limit of tolerance. Local application of cold was applied by a special apparatus for as long as 400 to 500 hours in several patients, at temperatures of 48° to 50° F. continuously except for short intervals when the areas were examined and necrosed tumour tissue removed from time to time. The tumour cells showed necrosis. Pain was relieved within 24 hours. General hypothermia was induced 14 times in 12 patients, 3 methods of applying external cold being used—ice packs, ice-bags, and the continuous-flow tub. Ice-bags were quite satisfactory for most patients, the other 2 methods being employed for those relatively obese. The room temperature was maintained at 45° to 50° F. A certain amount of narcosis is necessary and is obtained by nembutal in 1½ grain doses every half-hour until adequate narcosis is attained. Eleven patients were successfully hibernated, and, of these, 3 were alive 3½, 4½, and 8 months after hibernation. One patient died during hibernation, apparently from cerebral oedema superimposed on meningeal metastases.

Radiotherapy

Quantitative examination of human biopsy material.—The results of experimental work on the biological response of both normal and malignant cells to irradiation both *in vivo* and *in vitro*, carried out at the Strangeways Research Laboratory, Cambridge, by F. G. Spear, A. Glücksmann, and others, show that the reaction of the cells is essentially the same whether they are irradiated *in vitro* or *in vivo*. Small dose α or X-radiation is followed by a diminution in the number of cells entering mitosis, but the cells so hindered may recover from the effects of exposure and ultimately divide. The cellular changes vary—mitotic, differentiation, resting, degenerative—according to the circumstances of irradiation. Some squamous-celled carcinomas in man show an increase in differentiation, e.g. keratinization, after irradiation; this process, in cases successfully treated, is accompanied by disappearance of mitotic cells. An

analysis of human biopsies on squamous- and basal-celled carcinomas was undertaken by A. Glücksmann to see if the results of irradiation could be expressed quantitatively along the lines of previous work on animal (embryonic) tissues. For this preliminary paper 284 biopsies were made; one biopsy was taken before treatment and one or more after the first exposure. The reaction of malignant cells to irradiation differs from that of normal cells in degree rather than in kind; as in the case of normal tissues, exposure of malignant cells to irradiation is followed by inhibition of cell division: these cells may subsequently show mitosis and break down (nuclear degeneration) or they may attempt to undergo differentiation. A differentiating cell may eventually break down and disappear as a result of cytoplasmic degeneration. An unsuccessful attempt at differentiation may lead to increase in the size of the cell. Since a differentiating (or a monster) cell does not divide, any cell that behaves in this way as a result of irradiation is rendered harmless. The quantitative histological examination of human biopsy material provides a method by which the biological response of malignant cells to irradiation can be correlated with the physical conditions of exposure, e.g. it can be applied to studies on the significance of the time, intensity, and wave-length factors in irradiation. Since the effect of an irradiation depends upon the activity of cells at the time of exposure, a malignant tumour should be judged not only in terms of its pathological classification (including that of Broders) but also in terms of the number of cells in each of the categories (resting, dividing, differentiating, and degenerating) present at the time of irradiation. The efficacy of the exposure can then be judged by the quantitative differences in the counts made at various intervals during and after treatment.

Treatment of surrounding tissue.—S. Russ and G. M. Scott report experiments which showed that grafts of Jensen's rat sarcoma grew more readily in the normal tissue of a rat than in the adjoining tissue which had been exposed to X-rays or radium (irradiation of the tumour bed). When a dose of X-rays, approximately 1,200 roentgens, was given to the surrounding tissue of a rapidly growing Jensen's rat sarcoma, the rate of growth of the tumour was considerably slowed down, and nearly 37 per cent (30 out of 82 tumours) disappeared. The amount of damage to the skin thus caused was negligible, nothing more than slight temporary depilation in some rats. The number of untreated control tumours which spontaneously disappeared was 13 out of 190. It is pointed out that S. Handley attempted with some success to block the lines of spread of malignant disease by exposing the probable paths of dissemination by gamma-rays in a patient.

Genito-urinary system

Subarachnoid injections of alcohol.—F. L. Bauer treated 22 patients with incurable and advanced genital carcinoma associated with severe pain with subarachnoid injections of alcohol. When the pain distribution indicated involvement below the 11th thoracic cord segment, the injections occasionally gave excellent relief, but more often the relief was incomplete or of short duration. Such injections are often followed by serious permanent motor and sphincter disturbances. There is an apparent correlation between the degree of relief obtained and the amount of the resulting motor and sphincter disturbance.

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CARRIERS IN INFECTIVE DISEASE

See also B.E.M.P., Vol. II, p. 755; Cumulative Supplement, Key No. 215; and p. 13 of this volume.

Detection, Cure, and Care of Carriers

Use of liquid paraffin

Disinfection of hospital equipment.—M. Van den Ende and E. T. C. Spooner state that the application of a 30 per cent solution of liquid paraffin in white spirit to bed-clothes will reduce the number of dust-borne organisms in the air of a hospital ward, and will eliminate the great increase in the number of bacteria in the air which generally accompanies bed-making. The articles of clothing are immersed in the solution, wrung out, and spun in a hydro-extractor. The floors of wards should be scrubbed with the same solution.

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Ende, M. Van den, and Spooner, E. T. C. (1941) *Lancet*, **1**, 751.

CATARACT

See also B.E.M.P., Vol. III, p. 1; and Surveys and Abstracts 1939, p. 272; 1940, p. 243.

Acquired Cataract*Symptomatic cataract*

Associated with tetany and osteomalacia.—Under the title 'Cataract in Adult Rickets (Osteomalacia)' J. P. Maxwell and H. T. Pi, of the Peiping Union Medical College, revert to the subject of adult rickets and discuss the condition called *cataracta tetanica*, which had not been specially associated with osteomalacia, until Pi (1934) found that out of 60 well-marked examples of osteomalacia 13, or 22 per cent, had this form of cataract. This form of cataract must be specially looked for, because the ocular symptoms are slight, and the illiterate patients are not likely to complain of loss of vision until it is advanced. Tetany is common in osteomalacia. In some of the 13 tabulated cases the blood calcium is only slightly below the normal, whereas the blood phosphate is extremely low. The change may be due to parathyroidectomy (post-operative tetany) or occur in idiopathic tetany also of endocrine origin. From a review of previous knowledge of cataract in idiopathic tetany it appears that the cataract may be (1) lenticular opacities in pregnant women with tetany, (2) in pregnant women with rickets, and (3) in pregnancy with convulsions. Under appropriate treatment these cataracts improve, but do not disappear.

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CEREBROSPINAL FEVER

See also B.E.M.P., Vol. III, p. 39; Cumulative Supplement, Key No. 223; Surveys and Abstracts 1939, pp. 125 and 274; 1940, p. 244; and pp. 4 and 65 of this volume.

Clinical Picture*Meningococcal septicaemia*

Haemorrhage (Waterhouse-Friderichsen syndrome).—J. F. Hughes reports a case of fulminating meningococcal septicaemia associated with purpura and adrenal haemorrhage, the Waterhouse-Friderichsen syndrome, in a well-nourished female infant aged 10 weeks. The clinical picture of this condition is characteristic. Of the cases 70 per cent occur in infants under 2 years of age, and 90 per cent during childhood and adolescence. The picture is a combination of acute adrenal insufficiency and a fulminating infection, for example, purpura or fever. A previously healthy child suddenly collapses, with Hippocratic facies. There may be vomiting and hyperpyrexia. At the onset purpura is present, and these rapidly become extensive and even simulate post-mortem lividity. Meningitic signs are generally absent. As a rule death occurs within 24 hours of the onset. Treatment by a combination of chemotherapy for the infection, and adrenal cortical hormone for the acute adrenal insufficiency, is suggested.

W. H. Grace, C. V. Harrison, and T. B. Davie report 3 cases of haemorrhage into the adrenal cortex occurring in the course of meningococcal septicaemia, the Waterhouse-Friderichsen syndrome. The authors suggest that treatment should consist of the prompt administration of sulphapyridine in adequate dosage by mouth, or by intramuscular injection in comatose patients. Steps to combat the severe shock and to restore and maintain the blood pressure by transfusion of plasma or blood should be taken, and extracts of adrenal cortex should be given. The authors report a case of this syndrome in a woman of 40, who recovered with this treatment.

Diagnosis and Differential Diagnosis*Laboratory technique*

Opsonic index.—T. Houston and J. C. Rankin summarize their work on cerebrospinal fever since 1907. In the epidemic in Belfast in 1907–8 an application was devised of A. E. Wright's opsonic technique for the laboratory diagnosis of this infection. It was also employed in the war of 1914–18 and in a recent outbreak in Belfast. The first place in the differential diagnosis must be given to the isolation of the meningococcus from the cerebrospinal fluid or blood, but in a number of cases such examinations may fail to give positive results, and in cerebrospinal septicaemia without meningitis blood cultures may be negative. The technique, that of the opsonic index, is not difficult, and its validity depends on the fact that normal sera and sera from cases infected with microbes other than the meningococcus have very little opsonic and no agglutinative effect on the meningococcus. Positive films show high agglutination and phagocytosis. Other infections require most careful counts for opsonic index determinations, but in the case of meningococci such a laborious procedure is usually unnecessary. From examination of sera from several hundreds of patients the technique has been found to be reliable. It gives positive results in patients treated by sulphapyridine, and as this reaction is no doubt a reaction of immunity, its presence in patients thus treated is considered to support the view of Fleming and others that the action of such drugs is bacteriostatic and that the defences of the tissues are also necessary for a cure of the disease.

Complications and Sequelae*Double infection*

Meningococcus and B. enteriditis.—K. J. Guthrie and T. Anderson report an unusual case of double meningeal infection in an infant aged 14 months. The child was admitted to hospital with what proved to be a meningococcal meningitis. This was treated with sulpha-

thiazole which caused the temperature to fall to normal within 48 hours of beginning treatment, and lumbar puncture showed a clear fluid which did not yield meningococci. Progress was uneventful for a fortnight. The patient then became ill again, the temperature rose, and lumbar puncture gave a fluid with abundant Gram-negative bacilli. These organisms were shown to be members of the enteritidis group.

Treatment

Sulphapyridine and serum

J. M. Todesco reports on the combined use of sulphapyridine and anti-meningococcal antitoxin in 31 patients with cerebrospinal fever. Of these 7 died, mainly those admitted to hospital in a late stage of the disease. The dosage of sulphapyridine was 2 grammes, repeated in 4 hours, after which 1 gramme was given every 4 hours for 36 hours, and then 0.5 gramme 3 times a day for 24 hours. Children under 5 years of age received half this dosage. Lumbar puncture was performed on admission and repeated in 24 hours, if the pressure was much raised. This was combined with intrathecal injections of 20 to 40 cubic centimetres of anti-meningococcal antitoxin. The rapid improvement, especially relief of restlessness, headache, and delirium, was remarkable; the temperature fell to normal within 24 to 36 hours, and the rigidity diminished after 2 or 3 days. The author concludes that the combined treatment with sulphapyridine and serum is preferable to the use of sulphapyridine alone.

Sulphapyridine

D. T. Thomas reports a case of relapsing cerebrospinal fever in which the use of sulphapyridine was unsuccessful. A woman, aged 40, was admitted to hospital with meningococcal meningitis. She was given 3 doses of 2 grammes of sulphapyridine at 4-hourly intervals, then 1-gramme doses at similar intervals for 72 hours, and then 0.5 gramme 3 times a day for 2 days. On the fourth day the patient became free from symptoms and signs, and the cerebrospinal fluid was clear, sterile, and contained a normal amount of sugar. Fifteen days later the patient was readmitted with severe headache and vomiting. Meningococci were again found in the cerebrospinal fluid. A prolonged course of sulphapyridine was given, and followed by a course of sulphanilamide and anti-meningococcal serum. The patient, however, remained pyrexial, and died 5 weeks after readmission.

Sulphapyridine in mass dosage

Prophylaxis.—F. C. Gray and J. Gear found mass dosage with sulphapyridine to be an efficient means of controlling an epidemic of cerebrospinal meningitis immediately by reducing the carrier rate to negligible proportions and preventing the onset of the disease in those incubating the infection. The authors suggest that in the event of a case of the disease occurring in a semi-permanent military camp, the carrier rate should be determined if possible. If this exceeds 20 per cent, conditions are favourable for an epidemic and mass treatment with sulphapyridine is justified. If an epidemic is already present, mass dosage is justified without preliminary swabbing. The dose recommended is 1 gramme 3 times a day on 2 consecutive days. Ordinary hygienic precautions, especially the prevention of overcrowding, should not be neglected.

Sodium sulphapyridine

Cerebral symptoms.—D. F. Johnstone and P. Forgacs point out the danger of cerebral symptoms, identical with those of meningitis, arising from heavy doses of sodium sulphapyridine. Five cases of meningitis are described. Case 1: A boy aged 14 with purulent cerebrospinal fluid had 4-hourly injections of sulphapyridine (2 cubic centimetres) and 3-hourly injections of 3 cubic centimetres on admission. On the third day the fluid was clear, but clinical symptoms remained. The dose-frequency was reduced to 4-hour intervals but the patient died. Case 2: A baby aged 20 months was given $7\frac{1}{2}$ grains orally; 4 days after admission, 2 cubic centimetres were injected intramuscularly followed by 4-hourly doses of 1.4 cubic centimetres. By the eighth day the fluid was clear but clinical symptoms persisted. The dose was increased, then reduced to 3 cubic centimetres 12-hourly, but slight improvement was followed by death. Case 3: A girl aged 7 had intramuscular injections of 3 cubic centimetres 3-hourly for 2 days. When the fluid began to clear, the dose was reduced and omitted. Recovery was rapid, but renewal of the drug was followed by return of the symptoms and was finally omitted with permanent recovery. Case 4: The patient had similar treatment and results. Case 5: A girl aged 10 was given $22\frac{1}{2}$ grains by the mouth on admission and 15 grains 4-hourly for 48 hours. The meningeal signs, however, increased, and accordingly the drug was finally omitted, and an uninterrupted recovery followed. The view that this persistence of the symptoms is due to continued infection is untenable as fluid appearance is a reliable test and as the improvement on suspension of the treatment was so obvious. The toxic effect of the drug is suggested. As symptoms of the original disease and of those due to sodium sulphapyridine are indistinguishable, lumbar injections should be made in cases of doubt, or if symptoms persist after two or three days. Individual sensitivity to the drug appears to vary.

Sulphathiazole

H. S. Banks employed sulphathiazole after one or more preliminary doses of sulphapyridine in 52 cases of cerebrospinal fever, and sulphathiazole alone in 44 cases. There were 2 deaths in the whole series (2.1 per cent); this result compares favourably with previous series treated with serum and sulphanilamide or other sulphonamide drugs. The evidence so far suggests that this drug is at least equal in potency to sulphapyridine in meningococcal infections, and

that, with adequate dosage, bacteriostasis is complete and phagocytosis advanced within 12 to 24 hours. Concentration in the cerebrospinal fluid varies from about 15 to 40 per cent of that in the blood, and is rarely greater than 1.5 milligrams per 100 cubic centimetres. Nausea, vomiting, and dehydration, as well as other toxic effects, are rare. The initial daily dosage varies according to age from 3 to 9 grammes for the first few days; two-thirds of this dose is given for the next 2 days, and one-third for a further 2 days. The period of administration is 6 to 7 days, and the total amount of the drug is 40 or 50 grammes for an adult.

Banks, H. S. (1941) *Lancet*, **1**, 104.

Grace, W. H., Harrison, C. V., and Davie, T. B. (1940) *Lancet*, **2**, 102.

Gray, F. C., and Gear, J. (1941) *S. Afr. med. J.*, **15**, 139.

Guthrie, K. J., and Anderson, T. (1941) *Brit. med. J.*, **1**, 193.

Houston, T., and Rankin, J. C. (1940) *Ulster med. J.*, **9**, 61.

Hughes, J. F. (1940) *Brit. med. J.*, **2**, 353.

Johnstone, D. F., and Forgacs, P. (1941) *Brit. med. J.*, **1**, 772.

Thomas, D. T. (1940) *Lancet*, **2**, 297.

Todesco, J. M. (1940) *Lancet*, **2**, 196.

CEREBROSPINAL FLUID

See also B.E.M.P., Vol. III, p. 52; and Surveys and Abstracts 1939, p. 276.

Anatomy and Physiology

Pressure of the cerebrospinal fluid

Continuous recording.—F. F. Ellis describes an apparatus, called the 'cottonometer', for the continuous record of cerebrospinal fluid pressure levels by means of a graph. The author considers that it is essential to prevent cerebral oedema in acute cerebral trauma; this can be done by keeping the intracranial tension at a normal level by lumbar puncture. Even with blood-stained cerebrospinal fluid, lumbar puncture is not contra-indicated, since capillary oozing becomes less when the pressure is reduced to normal. In addition to the cortical damage that cerebral oedema may cause, it may also produce post-traumatic symptoms by the production of intracranial hypertension, the basis of which is probably some biochemical change associated with the oedema, perhaps liberation of excess protein into the cerebrospinal fluid with a consignment increase in the osmotic pressure.

Effect of histamine phosphate injections in alcoholic and psychotic patients.—D. E. Cameron and S. R. Rosen publish the result of intravenous injection of histamine phosphate on the manometrical pressure of the cerebrospinal fluid, which is evidence of the degree of reactivity of the smaller intracranial arteries, dilatation of the intracranial arteries causing increased pressure of the cerebrospinal fluid. The average rise in the pressure of the cerebrospinal fluid in 38 patients with senile psychoses was 34 millimetres of water, in 29 younger alcoholic psychotic patients 86 millimetres, and in 26 other psychotic patients 70 millimetres of water. It is clear that there is a definite diminution of reactivity of the cerebral arteries in the senile group in contrast to the group of younger patients. Increased reactivity of alcoholic patients is rather difficult to explain; it has been suggested that excessive alcoholism tends to reduce the probability of arteriosclerosis.

Pathology of the Cerebrospinal Fluid

Hydrochloric acid and collargol tests

W. Nagel describes the hydrochloric acid and collargol test (HCT) invented by C. Riebeling. This is a very simple colloidal test for the cerebrospinal fluid. The materials used are a 0.1 per cent solution of Heyden's collargol which will keep for about 2 months. The solution actually used is 0.01 per cent and must be freshly prepared. A hydrochloric acid solution N/500 is also required. Ten test tubes are used with 1 cubic centimetre of cerebrospinal fluid—hydrochloric acid mixture, the cerebrospinal fluid part being $\frac{1}{2}$, $\frac{1}{5}$, $\frac{1}{10}$, $\frac{1}{15}$, $\frac{1}{20}$, $\frac{1}{40}$, $\frac{1}{60}$, $\frac{1}{80}$, $\frac{1}{100}$ respectively. One cubic centimetre of 0.01 per cent collargol solution is then added to each tube and well shaken. The test is finished after 12–24 hours. Normally the liquid in the first tube is brown and transparent, and in the others colourless with a precipitate at the bottom of the tube. There is sometimes one tube with an intermediate (brown-opaque) state of the liquid. Collargol (brown) is precipitated by hydrochloric acid, and a water-clear liquid with a precipitate at the bottom of the tube should result. Cerebrospinal liquid acts as a protector and prevents precipitation. The author describes as a 'normal' picture when from one to four tubes remain brown, the rest being colourless. There is a 'subnormal' state of the cerebrospinal fluid when one or two intermediate test tubes are opaque. The fluid is definitely pathological when some colourless tubes are followed by brown ones again, and typical 'paralysis of the insane' series and 'meningitis' series are distinguished.

The new test is particularly useful in early stages of mental or neurological disease in which the cerebrospinal fluid tests are not effective.

Cerebrospinal Rhinorrhoea

Treatment

Bifrontal craniotomy.—A. W. Adson reports a case of cerebrospinal rhinorrhoea arising spontaneously in a woman, aged 34, who had been obliged thereby to give up her work as a teacher. It was cured by an operation Adson had previously performed, namely, bifrontal instead of the usual unifrontal craniotomy, thus allowing elevation of the dura mater in both

halves of the frontal fossa, and sacrifice of both olfactory lobes, with anosmia as the only resulting disadvantage of the operation. There was not any fracture, but there was a fistulous tract extending into the olfactory groove on the right side; this was closed by an accurate plastic operation. As a safeguard against meningeal infection from the operation, sulphanilamide, grains 90, was given for 4 days before operation, and a daily dose of 45 grains was given for 10 days after operation.

Adson, A. W. (1941) *Proc. Mayo Clin.*, **16**, 385.

Cameron, D. E., and Rosen, S. R. (1941) *Amer. J. med. Sci.*, **201**, 871.

Ellis, F. F. (1940) *Aust. N.Z. J. Surg.*, **10**, 20.

Nagel, W. (1940) *Schweiz. med. Wschr.*, **70**, 661.

Riebeling, C. (1938) *Klin. Wschr.*, **17**, 501.

CERVICAL RIB

See also B.E.M.P., Vol. III, p. 75; and Surveys and Abstracts 1939, p. 277; 1940, p. 245.

Anatomical Basis of the Symptoms

The brachial plexus

Use of procaine hydrochloride.—L. Kaplan reports on the injection of procaine hydrochloride into the scalenus anticus muscle in 40 patients to determine the origin of pain in the distribution of the brachial plexus, and finds that it is a satisfactory diagnostic procedure. The cases comprised 10 of the scalenus syndrome, 6 of the scalenus syndrome following trauma, 12 of subacromial bursitis with adhesions, 3 of calcification in the supraspinatus tendon, and 3 of other conditions about the shoulder. The measure is also of some therapeutic value when there is spasm of the scalenus anticus muscle of postural origin, due to trauma or to sub-deltoid bursitis of acute or chronic type. Repeated injections may obviate the necessity for scalenotomy.

Kaplan, L. (1941) *Arch. Surg., Chicago*, **42**, 739.

CHANCROID

See also B.E.M.P., Vol. III, p. 97; Cumulative Supplement, Key No. 227; Surveys and Abstracts 1939, pp. 155 and 277; 1940, pp. 91 and 245; and p. 109 of this volume.

Treatment

Sulphanilamide

O. Canizares and J. A. Cohen employed sulphanilamide in 114 cases of chancroid. In 64 cases of a small chancroid, cure was effected in 12 days. In 38 cases of large chancroid the drug was most effective, cure being complete in 18 days. In 11 cases of phagedaenic chancroids, 6 healed in an average of 27½ days, whereas the other 5 did not respond. In inguinal adenopathy, sulphanilamide does not control the formation of pus.

Canizares, O., and Cohen, J. A. (1940) *Arch. Derm. Syph., N.Y.*, **42**, 649.

CHICKEN-POX

See also B.E.M.P., Vol. III, p. 103; Cumulative Supplement, Key No. 228; and Surveys and Abstracts 1940, p. 246.

Complications

Neurological complications

M. G. Masten reports 2 cases of chicken-pox with neurological complications. The onset of these complications occurred 7 and 9 days respectively after the appearance of the eruption. In both cases the exanthem was extensive. Paralysis appeared in the lower extremities and progressed rapidly upwards, and was accompanied by pain, the latter being more severe in one of the cases. One case resembled neuronitis, and would be classified as a form of polyneuritis. Recovery from the neurological symptoms occurred in both cases.

Associated Diseases

Pemphigus acutus

J. Schwartzman reports a case of chicken-pox, in an infant of 4½ months, complicated by acute pemphigus, and ending fatally. It is suggested that there were grounds for the virus aetiology of pemphigus acutus. Purposeful exposure of non-immune children, or careless isolation because of the usual mildness of chicken-pox cases, is unjustifiable.

Masten, M. G. (1940) *Arch. Pediat.*, **57**, 749.

Schwartzman, J. (1940) *Arch. Pediat.*, **57**, 595.

CHOREA

See also B.E.M.P., Vol. III, p. 204; Cumulative Supplement, Key No. 237; and Surveys and Abstracts 1939, p. 278.

Treatment

Fever therapy and vitamin B

S. Stone treated 20 severe, moderately severe, and mild cases of chorea; of these, 7 severe cases were treated by artificial fever, together with vitamin B complex orally and aneurin chloride parenterally. One severe and one moderately severe case received aneurin chloride parenterally and vitamin B complex orally, all the others receiving vitamin B complex by

mouth. In the cases treated by artificial fever recovery occurred after about 14 hours of fever at 104° F. or higher. When this was combined with vitamin B therapy, advanced cardiac disease did not contra-indicate the fever treatment. There was generally a change for the better in the carditis at the end of treatment. One of the two patients treated with aneurin chloride responded with cessation of symptoms after the second intravenous injection of 10 milligrams of the drug. In the moderately severe and milder cases which all received 4 to 8 cubic centimetres of vitamin B complex orally, 3 times daily, the improvement in physical manifestations was less rapid than in the fever-treated cases, but most of the symptoms disappeared within a month.

Stone, S. (1940) *New Engl. J. Med.*, **223**, 489.

CHORION-EPITHELIOMA AND HYDATIDIFORM MOLE

See also B.E.M.P., Vol. III, p. 216; and Surveys and Abstracts 1940, p. 246.

Chorion-epithelioma

Diagnosis

Extra-genital chorion-epithelioma in male.—J. F. Erdmann, H. A. Brown, and H. W. Shaw report a case of extra-genital chorion-epithelioma in a man aged 45; histological examination of numerous serial blocks of the testis failed to show a primary testicular tumour. Only 4 similar cases have been reported. A valuable diagnostic point is the development of gynaecomastia in an apparently healthy male. In this case the presenting symptom was a breast tumour. The Aschheim-Zondek test was negative, indicating that the test is not an infallible diagnostic procedure.

Hydatidiform Mole

Incidence, treatment, and clinical course

J. E. Giesen reviews 16 cases of hydatidiform mole, including 5 personal cases. The immediate risk of haemorrhage was found to be considerable. Post-operative haemorrhage and torsion of ovarian cysts were not uncommon. The former generally indicated the retention of a portion of the mole, and calls for further exploration. The incidence of chorion-epithelioma varies considerably. Of 3 cases in which spontaneous expulsion of the mole occurred, one patient was cured, one was curetted for persistent bleeding 3 months later, and one eventually underwent hysterectomy for a perforating mole. Of 11 patients treated by conservative measures, two died in hospital, one from septicaemia and the other from cerebral embolism. Two of the remaining 9 patients required further curettage, and two submitted to hysterectomy later. These results suggest that, apart from the possibility of chorion-epithelioma, many debilitating symptoms may follow even the simplest case of hydatidiform mole.

Erdmann, J. F., Brown, H. A., and Shaw, H. W. (1941) *Urol. cutan. Rev.*, **45**, 1.
Giesen, J. E. (1941) *N.Z. med. J.*, **40**, 3.

CLIMACTERIC AND ITS DISORDERS

See also B.E.M.P., Vol. III, p. 228; Cumulative Supplement, Key Nos. 242 and 243; and Surveys and Abstracts 1939, p. 279; 1940, p. 247.

The Climacteric in the Female

Clinical picture

Hyperthyroidism associated with the menopause.—Six cases are described by M. G. Wohl and N. Pastor to illustrate the relation between the menopause and the thyroid. Experimental work on animals had previously shown that castration may lead to hyperthyroidism, and that injections of the urine from women at the menopause may have the same effect. Conversely a lowered metabolism has been induced by injections of oestrogen in ovariectomized and normal animals. The 6 patients showed symptoms of hyperthyroidism, based on the metabolic rate, vasomotor reactions, and the condition of the thyroid. There were other abnormalities. Two patients underwent thyroidectomy which failed to abolish the symptoms, and in them post-operative myxoedema developed. Two were given respectively progesterin, one international unit injected 3 times a week, and oestrogen, 2,000 rat units twice a week, but without any surgical treatment. They made satisfactory recoveries. The sixth had combined manifestations of thyrotoxicosis and menopause and required partial thyroidectomy. The recovery was completed only when oestrogen was given. The authors conclude that symptoms of hyperthyroidism during the menopause are misleading and may lead to unnecessary surgery. Oestrogen therapy should first be tried.

Treatment

Oestradiol implantation.—G. H. Twombly and R. S. Millen report the effects of treatment of 37 menopausal patients, 4 cases of kraurosis vulvae, 4 cases of leucoplakia buccalis, and 1 case of adeno-genital hirsutism by implantation of solid crystals or pellets of oestrone or oestradiol. They found that oestrone was ineffective whereas 25 milligram pellets of oestradiol successfully prolonged alleviation of menopausal symptoms. The dose necessary was a total of 1-3 pellets inserted intramuscularly at intervals of a month. The full effect became apparent in about a month, and lasted 5 months to a year. The treatment is contra-indicated in women with intact uteri, since it caused bleeding in 9 out of 12 patients treated. Bleeding did not occur in patients who had undergone castrating doses of radium some time previously. The

treatment was only partially effective in the cases of kraurosis, and no improvement occurred in the case of hirsuties.

Use of oestrone and progesterone in diabetic cases.—E. Cantilo employed oestrone and progesterone in large doses in 40 women during the menopause or post-menopause with diabetes mellitus. All these patients showed evidence of a disturbed hormonal balance characterized by pituitary hyperactivity. Some of the cases were severe, with ketonuria. When insulin treatment and diet were employed without any other endocrine therapy, the disturbed carbohydrate metabolism remained almost unchanged. The dosage of oestrone was 5 to 15 milligrams 3 times a week and that of progesterone up to 10 milligrams 3 times a week. Insulin was not given and dietary restrictions were not enforced. Successful results were obtained in all cases.

Stilboestrol.—L. Kurzrok, C. S. Birnberg, and H. Weber report on the use of stilboestrol in 122 women with menopausal symptoms. Successful results were obtained in 64 per cent of cases. Toxic manifestations occurred in many of the patients, the most frequent being nausea. The total dosage in some cases was 200 milligrams during a period of 2 to 3 months.

Oestrin, psychotherapy, and sedation.—C. H. Lawrence and A. C. Moulyn state that the symptoms associated with the menopause are in a small minority only sufficiently severe to make patients consult a medical practitioner. A positive test for prolan in the urine was found in 48 only out of 100 women admitted to hospital for severe menopausal symptoms. In 81 per cent of this group the symptoms were chiefly those of vasomotor instability, and 90 per cent of these patients were benefited by oestrin therapy. In the patients in whom the urinary prolan was negative, treatment with oestrin brought relief in 25 per cent only, whereas simple psychotherapy or sedation was beneficial in over 80 per cent. There was not any apparent relation between the presence or absence of oestrin alone and the character or severity of symptoms.

Endocrine therapy.—R. E. Hemphill and M. Reiss report on the state of endocrine function in 30 cases of depression occurring at the menopause. They found symptoms of ovarian, thyroid, and adrenal dysfunction in different individuals in varying degree, so that the cases could be classified according to the predominating glandular disturbance. The response of a number of patients to follicular, luteal, and corticotrophic hormone was tested. Favourable results with follicular hormone were observed only in patients of two groups, namely, hypo-ovarian, and hypo-ovarian combined with hyperthyroid. The indiscriminate use of follicular hormone may be harmful if thyroid insufficiency is present. The authors consider that disturbances of the activity of the anterior lobe of the pituitary are largely responsible for the protean characteristics of involutional melancholia.

The Question of a Climacteric in the Male

Symptoms

Senile keratoderma.—C. Henschen describes hyperkeratosis of the palms and soles in a diabetic elderly patient; fissures in the hardened skin were very painful. The author tried injections of 5 milligrams each of oily perandren solution, and after 8 injections the thick and hardened skin disappeared and normal rosy skin appeared. It is suggested that the condition is that described by H. W. Barber as symmetrical hyperkeratosis of palms and soles. Barber's and other authors' patients are described as elderly persons with climacteric symptoms. There is also a certain connexion with gout or gouty metabolic disturbances, and perhaps with diabetes mellitus. In patients with gouty metabolic disturbances the skin changes might be caused by production of uric acid, or molecular equivalents of tophi, which cannot be excreted through the cutaneous glands and therefore accumulate under the skin of soles and palms. The connexion between the climacteric and the skin changes is not quite clear, but it is concluded—*post hoc propter hoc*—from the study of the effect of perandren (testosterone) in the author's case, that such an association exists.

Barber, H. W. (1933) *Proc. R. Soc. Med.*, **26**, 497.

Cantilo, E. (1941) *Endocrinology*, **28**, 20.

Hemphill, R. E., and Reiss, M. (1940) *J. ment. Sci.*, **86**, 1065.

Henschen, C. (1940) *Schweiz. med. Wschr.*, **70**, 690.

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Lawrence, C. H., and Moulyn, A. C. (1941) *New Engl. J. Med.*, **224**, 845.

Twombly, G. H., and Millen, R. S. (1941) *Surg. Gynec. Obstet.*, **72**, 605.

Wohl, M. G., and Pastor, N. (1941) *Amer. J. Obstet. Gynec.*, **41**, 792.

COELIAC DISEASE

See also B.E.M.P., Vol. III, p. 262; Cumulative Supplement, Key No. 247; and Surveys and Abstracts 1939, p. 282.

Pathogenesis and Aetiology

Occurrence in identical twins

Dorothy Collishaw records coeliac disease in 2 male identical twins aged 2 years. Analysis of their faeces showed excessive fat, and after a fat-free diet for 2 months the infants improved. This occurrence suggests that the inability to absorb fat may be an inborn digestive defect.

Clinical Picture*Hypovitaminosis of fat-soluble vitamins*

F. Albright and J. D. Stewart report hypovitaminosis of all the fat-soluble vitamins due to steatorrhoea in a woman 35 years of age. Chronic regional ileitis was presumably the initial lesion and led to functional insufficiency of the intestines. This resulted in severe steatorrhoea, which in time prevented absorption of all the fat-soluble vitamins. There resulted hypovitaminosis D with hypocalcaemia, hypovitaminosis K with a severe bleeding diathesis and failure of the blood to clot, hypovitaminosis A with a low serum content of carotenoids, the precursor of vitamin A, and xeroderma, and probably hypovitaminosis E, although there was no clinical or laboratory evidence of this condition. It is also possible that the steatorrhoea led to a disturbance in the steroid metabolism which resulted in an absence of 17-ketosteroids from the urine. Moreover, because of a deficiency in the protein metabolism, the patient developed pituitary amenorrhoea with an absence of follicle-stimulating hormone in the urine. Finally, the intestinal anastomoses that were necessitated also led to a primary anaemia in spite of the presence of free hydrochloric acid in the gastric contents. Patients with chronic steatorrhoea should receive a low fat diet, and fat-soluble vitamins in fat-free vehicles. In this case the vitamin K deficiency responded dramatically within 24 hours to the oral administration of 1 milligram of 2-methyl-1:4-naphthoquinone in oil of maize, the plasma prothrombin concentration rising from 15 to 60 per cent of normal.

Haemorrhagic diathesis

Vitamin K deficiency.—R. Kark, A. W. Souter, and J. C. Hayward describe a haemorrhagic diathesis distinct from scurvy, occurring in a patient with idiopathic steatorrhoea. This haemorrhagic condition was ascribed to hypo-prothrombinaemia as a result of vitamin K deficiency, and was corrected by the administration of synthetic vitamin K. The salient features of haemorrhagic hypo-proteinaemia are 'needle-puncture' and other subcutaneous haematomas, persistent haemorrhage from wounds, haemorrhages from the mucous membranes, and occasionally haemarthroses. Laboratory tests showed a markedly reduced blood-prothrombin concentration, below 20 per cent of normal, and some prolongation of the blood coagulation time, which is rarely extreme. This haemorrhagic condition appears in steatorrhoea only after prolonged treatment with almost complete restriction of fatty foods which greatly diminishes the intake of the fat-soluble vitamin K. It is advisable to supplement such therapeutic alterations in diet with maintenance doses of vitamin K, or one of its analogues. One milligram of 2-methyl-1:4-naphthoquinone daily by mouth was found to be adequate in the case reported.

Diagnosis*Vitamin A absorption test*

According to C. D. May and J. F. McCreary, a constant feature of coeliac disease is a low rise in the level of vitamin A during the vitamin A absorption test. A similar low rise in the vitamin A absorption test often occurs in other conditions, which may, as a secondary effect, give the clinical appearances of the coeliac syndrome. The vitamin A absorption test is not specifically diagnostic for coeliac disease and is of limited value in the differential diagnosis of coeliac disease from other conditions producing the coeliac syndrome. It may be of value in following the clinical progress of recovery from the disease, since it appears to return to normal when recovery is complete.

Treatment*Synthetic vitamin K*

J. G. Allen writes on the comparative prothrombin responses to vitamin K and several of its substitutes in a case of non-tropical sprue, in a woman aged 31 who was under observation for 8 months and during that time was treated for a severe and often recurring haemorrhagic tendency. This might have been due to deficient absorption from the intestine of fat-soluble vitamin K; in this patient the jejunum, terminal ileum, and colon showed oedema radiologically. But the response to prothrombin was very slow, as it is in hepatic cirrhosis and not as rapid as it is when deficient absorption of vitamin K is corrected. It is possible that in this case the prothrombin deficiency was caused by impairment of the hepatic elaboration of prothrombin as well as to poor absorption of vitamin K from the intestine. There was not, however, any other evidence of liver insufficiency. The anti-haemorrhagic treatment in this case included the following courses: alfalfa concentrate (natural vitamin K), 2 courses; 2-methyl-1:4-naphthoquinone, 2 courses; an aqueous soluble sulphonated 2-methyl-1:4-naphthoquinone, 1 course (given parenterally); and 2-methyl-3-phytyl-1:4-naphthoquinone (synthetic vitamin K), 1 course. The conclusion was reached that natural (alfalfa concentrate) and synthetic (2-methyl-3-phytyl-1:4-naphthoquinone) vitamin K were considerably less active than the 2-methyl-1:4-naphthoquinone.

Albright, F., and Stewart, J. D. (1940) *New Engl. J. Med.*, **223**, 239.

Allen, J. G. (1941) *New Engl. J. Med.*, **224**, 195.

Collishaw, Dorothy (1940) *Brit. med. J.*, **2**, 904.

Kark, R., Souter, A. W., and Hayward, J. C. (1940) *Quart. J. Med. N.S.*, **9**, 247.

May, C. D., and McCreary, J. F. (1941) *J. Pediat.*, **18**, 200.

COLDS

See also B.E.M.P., Vol. III, p. 271; and Surveys and Abstracts 1939, p. 283.

Preventive Measures*Intranasal vaccine spray*

T. E. Walsh found that the prevention of colds by the use of subcutaneous vaccines was disappointing. Experimental evidence shows that the rational method of vaccination against so local a disease as a cold is by the local application of the vaccine to the nasal mucosa. The results of such vaccination in 384 patients over a period of 8 years are given. Of a total 627 patient-years of vaccination there were 74 per cent good results, 10 per cent fair results, and 16 per cent failures. A vaccine containing a mixture of organisms was blown into the nose by the patient each night from an atomizer; 6 puffs of the vaccine were sniffed up into each nostril. This was done each night for 3 weeks, and again, after a week's rest, for 2 weeks, and continued for alternate 2-week periods for the remainder of the 'cold year'. The author concludes that this method offers the best prophylaxis against the common cold.

Cold vaccines

Negative results.—H. S. Diehl, A. B. Baker, and D. W. Cowan report the results obtained from the use of the usual heat-killed bacterial vaccines for the prevention of the common cold. During the year of the investigation those who had received the vaccine reported an average of 2.1 colds per person. A control group which had not received any vaccine, but only a physiological solution of sodium chloride, reported an average of only 1.9 colds during the year of study. From this there is not any evidence that the vaccine had any influence on the average number of colds per person.

Treatment*Essential unsaturated fatty acids*

Negative results.—E. M. Boyd and W. F. Connell report on the effect of a purified concentrate of linseed oil, containing linoleic and linolenic acids, on the common cold. This essential fatty acid preparation contains little or no vitamin A or D. It was given to groups of patients for various periods, and capsules containing liquid paraffin were given to control groups. The authors conclude that the preparation has not any value in the treatment of the common cold.

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Diehl, H. S., Baker, A. B., and Cowan, D. W. (1940) *J. Amer. med. Ass.*, **115**, 593.

Walsh, T. E. (1940) *Ann. Otol., etc., St. Louis*, **49**, 875.

COLITIS

See also B.E.M.P., Vol. III, p. 292; and Surveys and Abstracts 1939, p. 286; 1940, pp. 26 and 249.

Ulcerative Colitis*Pathogenesis*

In relation to lymphopathia venereum.—E. C. Rodaniche, J. B. Kirsner, and W. L. Palmer, on the grounds that recent reports suggest that some cases of proctitis and ulcerative colitis may be due to lymphopathia venereum, investigated 34 cases of chronic ulcerative colitis and proctitis by means of Frei tests and neutralization tests. Of these 34 cases, 32 (94 per cent) gave negative Frei tests and did not show any evidence of neutralizing antibodies in their sera against the virus of lymphopathia venereum. In the 2 Frei-positive cases the virus could not be isolated from the intestinal lesions. The authors conclude that lymphopathia venereum and non-specific ulcerative colitis are independent diseases which, in their early stages, may resemble each other clinically and proctologically.

Clinical picture

General review.—D. Barlow discusses the problems of diagnosis and treatment of simple ulcers of the caecum, colon, and rectum illustrated by 50 published cases and 2 personal case reports. Although the caecum is the commonest site of ulceration, the caecal ulcer is not a specific entity. Other parts of the colon, particularly regions of relative stasis, for example, the sigmoid, are often ulcerated. The ulcers are usually funnel-shaped, perforated, with hard edges (suggesting slow onset) and muscular erosion. Ulcers of the stomach, caecum, ascending and sigmoid colon, all static areas, are similar in structure. In none of the cases under consideration was diagnosis correct. Indications for operation are clear in ulcers of the caecum and ascending colon, but not in other regions. All patients not operated upon died. Symptoms are not specific, but inexplicable pain, often mistaken for appendicitis pain, on the right side may indicate ulceration. Most patients are well nourished. There is often free gas after perforation, and constipation and vague pains before perforation. Simple drainage is inadequate and treatment should always be operative. The author suggests a resection with lateral anastomosis for a non-perforated ulcer and over-sewing or exteriorization for perforated ulcers. Local excision and suture with drainage of the pelvis are often successful.

T. T. Mackie, whose work on this subject began in 1931, defines chronic ulcerative colitis as a cyclical recurrent disease, of multivalent, complex, and incompletely known aetiology, characterized by successive phases of activity and quiescence, which may recur irrespective

of treatment. His early investigation of some 200 specimens of the bacterial flora did not give satisfactory evidence that any one of the numerous bacteria isolated is the specific micro-organism, and he concluded that positive agglutination reactions unsupported by confirmatory bacteriological evidence does not constitute valid proof; the diagnosis of bacillary dysentery can be substantiated only by isolation of the micro-organism. A negative conclusion was also reached about the therapeutic value of anti-dysenteric bacteriophage. Secondary changes occur in the alimentary tract in chronic ulcerative colitis, such as those causing anacidity or hypo-acidity. His observations show that hypermobility is much less frequent than hypomobility, and that a barium meal may remain in the ascending colon in spite of frequent evacuations, the paradox of constipation in the presence of diarrhoea. The proximal colon fails to empty at the normal rate, and this is accompanied by overactivity and spasm of the distal portion, with the resulting frequent small evacuations of blood, mucus, and pus. Multiple mixed deficiency states were noted at one time or another in 107 out of 200 patients. They are the result, not the cause, of the colitis, but when unrecognized or improperly treated are progressive and may become the dominant factor. They are due to inadequate supply of vitamins and biologically complete protein and mineral salts; there are several factors concerned, such as the diet, especially (a) the 'smooth' conventional diet of the colitis patient, and (b) morbid changes in the gastro-intestinal mucosa. A problem much investigated by the author is the sensitization of the colon by food protein; out of 150 patients 90 gave subjective, and 86 objective, evidence of sensitization of the colon to certain foods. The natural cycle of chronic ulcerative colitis, divided into 4 phases, shows (1) the active disease due to one of several non-specific infections with only one common characteristic, invasive power of overcoming the host's resistance and so allowing secondary infections to occur; the accompanying inflammation tends to fix in the affected tissues antigenic foreign protein of bacterial and dietary origin; in this phase the so-called allergic factor is most easily identified. Phases 2 and 3, respectively convalescence and quiescence, show the least evidence of the allergic factor; phase 4 shows recurrence of active disease and more evidence of sensitization. Treatment must be based on the multivalent mechanism; infection should be met by autogenous vaccines or the newer chemotherapeutic remedies of which sulphathiazole is the most promising. All dietaries should be high in protein and in natural vitamin sources, and low in sugar and starches. Hydrochloric acid should counter achlorhydria. For inactivity of the ascending colon a single large dose of castor oil should be followed each morning by a small dose of sodium sulphate. Of 146 patients treated solely by medical measures, in 42, or 29 per cent, the disease was apparently arrested for periods ranging from 4 months to 6 years, 58 were improved, 41 were not benefited, and 5 died. In view of the number of failures surgical treatment is discussed with wise caution.

Treatment

Sulphonamide compounds.—E. N. Collins reports on the use of sulphonamide compounds in 44 cases of chronic ulcerative colitis. In most cases in which sulphanilamide was employed, it was given by a retention enema. A 45 grain powder of sulphanilamide is dissolved in a pint of warm distilled water, and one-quarter given 4 times daily. Treatment is given for 10 to 14 days, then on alternate weeks in courses of 2 or 3 months with an interval of 1 to 3 months after each course. When neoprontosil was used, it was given by mouth in an initial dosage of 15 grains, 1 hour before each meal, at bed-time, and at 3 a.m. When improvement occurred, the 3 a.m. dose was omitted. In a general survey of 26 cases, non-toxic and toxic, favourable responses were obtained in 15, or 57 per cent. The author believes that the drug has a place in the treatment of chronic ulcerative colitis, but should be considered as an adjunct to the usual forms of treatment, and not as a specific remedy.

Barlow, D. (1941) *Brit. J. Surg.*, **28**, 575.

Collins, E. N. (1940) *Ann. intern. Med.*, **14**, 55.

Mackie, T. T. (1941) *Trans. Studies Coll. Phys. Phila.*, 4 ser., **9**, 1.

Rodaniche, E. C., Kirsner, J. B., and Palmer, W. L. (1940) *J. Amer. med. Ass.*, **115**, 515.

COLON, CARCINOMA OF

See also B.E.M.P., Vol. III, p. 317; Surveys and Abstracts 1939, p. 288; 1940, p. 250; and p. 14 of this volume.

Diagnosis

Large intestine

Incidence and symptoms.—Records of 416 cases of carcinoma of the colon were collected by R. E. Buirge from necropsies, the ratio of male to female subjects being 1.77 to 1. The average age was 50 years and 6 months, the period of highest incidence being from 50 to 80 years. The most common sites were the sigmoid flexure, rectum, and caecum, rectal cancer being commoner in males. Delay in diagnosis had been considerable and due to the patients' reluctance to seek advice and to absence of pathognomonic symptoms. The average interval between onset of symptoms and diagnosis was 13 months for the ascending colon, 12½ months for the transverse and descending colon, and 14 months for the sigmoid flexure. A wrong diagnosis was made in 31 per cent of the cases, the commonest being that of appendicitis (for rectal cases) and anaemia. Symptoms included change of intestinal habit, in 62.3 per cent of the cases; diarrhoea alternating with constipation, in 27 per cent; nausea and

vomiting mostly in cases of caecal or sigmoid growth; painful defaecation, in 7.7 per cent; loss of weight at a late stage, in 85 per cent of the cases. The last symptom when accompanied by abdominal disturbances is useful in diagnosis in middle-aged patients. Obstruction, haemorrhoids, anaemia, especially in caecal cases, general distress, localized pain, and gross bleeding were frequent. The last demands immediate attention. The tumours were mostly palpable, especially in the proximal region. Diagnosis by biopsy, though important, is not by itself reliable. Frequent X-ray examinations gave a correct diagnosis in 87 per cent of the cases, and the sigmoidoscope was used for the recognition of cancer in the distal region. Metastases occurred in 57 per cent of the cases, especially in the liver, lymphatic glands, peritoneum, lungs, and intestine. In 43 per cent of the cases subjected to surgical treatment the cancer was confined to the colon: 50 per cent of the deaths could be attributed to pneumonia and peritonitis. Although the clinical history of the disease cannot be analysed from post-mortem records alone, such data may be valuable.

Clinical Picture

Multiple primary polypi

L. R. Schweiger and J. A. Barga report 23 cases from the records of the Mayo Clinic since Barga and F. W. Rankin's account of the subject in 1930, and divide them into 2 groups: (i) synchronous, in which multiple growths occur simultaneously, 16 cases, and (ii) metachronous, in which multiple carcinomas occur at different times, 7 cases. From this series are excluded cases of multiple polypi of low grades of malignancy and single lesions that grossly were undoubtedly carcinomatous and associated with single polypi of a low grade of malignancy. The cases of 2 malignant lesions of the colon, especially in group (i), are of practical importance because the presence of another growth, after removal of the more obvious of the two growths, is responsible for poor results of the removal of one growth. It is regarded as probable that in many instances multiple independent lesions are not recognized. The suggestions that apparently independent multiple growths are due to extension of one tumour and of implantation are critically considered; criteria are quoted for extensions of one growth and it is concluded that transplantation from one site to another in the colon is extremely rare.

Treatment

Surgery

One stage resection advantages.—C. W. Mayo summarizes the analysis made in conjunction with W. R. Lovelace of 885 cases of malignant disease of the caecum, ascending colon, and hepatic flexure of the colon, but no further, operated upon or seen at the Mayo Clinic from 1907 to 1938. In 40 per cent of the cases the growth was in the caecum, and in 60 per cent in the ascending colon and hepatic flexure. In 590, or 67 per cent, of the 885 cases resection was performed with a view to cure. A patient with anaemia of undetermined origin should be examined radiologically. In 15 per cent of the 885 cases appendicectomy had been performed after the onset of symptoms attributable to the lesion in the right colon. As regards the age incidence, only in a little more than 2 per cent of the cases was the age less than 30 years; it is therefore suggested that whenever an operation is performed for appendicitis on a patient over 30 years of age, the incision should be large enough to allow examination of the ascending colon. Present-day surgical opinion favours the multiple-stage operative procedure rather than any single-stage operation. In these 590 cases a one-stage resection was performed in 315, and two-stage or multiple-stage procedures employed in 275. Analysis of the hospital mortality indicated advantages for the one-stage operation in which the percentage was 22.2 as compared with 28.9 for the two-stage procedure; it is suggested that 'the more stages required to complete the operation, the higher the operative mortality'. It was found that ileostomy, far from being a safety factor, was performed with additional risk. This review is admittedly in a sense a defence of the one-stage resection of the ascending colon; on an average it carries a lower hospital mortality rate and lower morbidity; it also removes the carcinoma from the body at a time earlier than in any multiple-stage operation.

Barga, J. A., and Rankin, F. W. (1930) *Ann. Surg.*, **91**, 583.

Buirge, R. E. (1941) *Arch. Surg., Chicago*, **42**, 801.

Mayo, C. W. (1941) *Proc. Mayo Clin.*, **16**, 67.

— and Lovelace, W. R. (1939) *Trans. West. S.A.*, **49**, 378.

Schweiger, L. R., and Barga, J. A. (1940) *Arch. intern. Med.*, **66**, 1331.

CONCUSSION AND COMPRESSION

See also B.E.M.P., Vol. III, p. 355; Cumulative Supplement, Key No. 255; Surveys and Abstracts 1939, p. 289; 1940, pp. 70 and 251; and p. 92 of this volume.

Concussion

Theory of concussion

K. C. Dixon suggests that concussion is due to compressional displacement of the nutritive cerebrospinal fluid from the interstices of the brain along the perivascular continuations of the subarachnoid space. This would deprive the nervous tissues suddenly of the sugar which is essential for their normal action, and would thus be responsible for the transient interruption of cerebral function seen in concussion.

Treatment of complications

Scalp wounds.—W. McKissock and B. Brownscombe report 53 cases of apparently trivial head injuries; many of the patients had scalp wounds, but none had fracture of the skull. An operation had been performed elsewhere on 27 of the patients, but primary healing had occurred in only 2; many had retained foreign bodies, most had only an inch of scalp shaved round the wound, and widely separated through-and-through sutures, generally of fishing gut, had been used. An abnormally high or low intercranial pressure was found in 19; in 16 blood was present in the cerebrospinal fluid; and in 41 there were abnormal physical signs referable to the central nervous system. Lumbar puncture did not increase intracranial bleeding. According to the authors the scalp wound should be treated by wide shaving of the scalp, cleansing, total excision of damaged tissue and removal of foreign bodies, and suture of the galea and skin in two layers without tension by closely approximated silk sutures.

Dixon, K. C. (1940) *Lancet*, 2, 360.

McKissock, W., and Brownscombe, B. (1941) *Lancet*, 1, 593.

CONJUNCTIVA, INJURIES AND DISEASES

See also B.E.M.P., Vol. III, p. 365; Cumulative Supplement, Key No. 256; and Surveys and Abstracts 1939, pp. 128 and 289; 1940, p. 251.

Non-Bacterial Inflammation*Inclusion conjunctivitis*

Sulphanilamide therapy.—P. Thygeson found that sulphanilamide was effective in causing rapid healing of inclusion conjunctivitis in infants and adults, as well as of the experimental disease in monkeys and baboons. Adults with predominant papillary hypertrophy responded more rapidly than those with predominant follicular hypertrophy. After the third day of treatment, the characteristic epithelial cell-inclusions could not be found. The dosage was $\frac{1}{2}$ to $\frac{1}{4}$ grain (0.02 to 0.03 gramme) of the drug per pound of body weight daily for 10 days.

Ophthalmia nodosa

Aetiology.—F. N. Knapp reports a case of ophthalmia nodosa in a woman 35 years of age. This condition, which is usually due to entry into the eye of caterpillar hairs, gives rise to itching, burning, and photophobia, and later to nodules, in the centre of which is a hair, on the cornea. In the author's case the disease appeared to be due to contact with hairy moss in which the patient had transplanted flowers some weeks previously.

Inflammation due to Bacterial Infection*Ophthalmia neonatorum*

Sulphapyridine.—J. S. du Toit describes the treatment of 32 cases of ophthalmia neonatorum with sulphapyridine. Doses of $\frac{1}{2}$ grain per pound of body weight, 3 times daily in addition to local treatment, were given. In several cases improvement occurred within a few hours. In all cases the immediate clinical improvement was good, and the purulent discharge soon diminished. Oedema of the lids and conjunctival chemosis rapidly subsided. In none of the cases did corneal complications follow.

Tumours and Pseudo-Tumours*Limbal tumours*

Malignant melanoma of conjunctiva.—G. T. W. Cashell records a case of malignant melanotic growth arising in diffuse pre-cancerous melanosis in a woman aged 70 years, who did not present any melanotic growth elsewhere or neurofibromatosis, but had an arterial blood pressure of 230/130 millimetres of mercury and arteriosclerosis. There was a history of a 'pigmented papilla' in her mother and a brother. In 1934 she showed dark-brown pigmentation of the conjunctiva, at the limbus and in the corneal epithelium of the right eye; this increased until in October 1939 a change occurred, with the appearance of a tumour on the limbus corneae. This and a melanoma in the lower fornix were removed, and reported to be malignant melanomas; after this report the right orbit was exenterated and the lids removed. The growths were composed of closely packed cells, round to spindle-shaped, a few pigmented, with mitoses, the tumour of the limbus being more actively growing than the other melanoma. In this case there was first acquired diffuse melanosis of the conjunctiva, of which 8 cases were recorded by Reese under the name of pre-cancerous melanosis; the average age at which the pre-cancerous condition is recognized is 48, and the interval before it becomes malignant 5 years; it must not be confused with congenital melanosis of the eyeball or conjunctiva. Diffuse melanosis begins in the basal layers of the epithelium, and, according to Masson, the melanotic tumours are neuro-epithelial in origin, associated with the specialized sensory nerve endings, which in the conjunctiva are the tactile corpuscles of Krause.

Cashell, G. T. W. (1940) *Proc. R. Soc. Med.*, 33, 545.

Knapp, F. N. (1940) *Arch. Ophthalm.*, N.Y., 24, 535.

Masson (1931) *Ann. Surg.*, 93, 218.

Reese (1938) *Arch. Ophthalm.*, N.Y., 19, 354.

Thygeson, P. (1941) *Arch. Ophthalm.*, N.Y., 25, 217.

du Toit, J. S. (1941) *S. Afr. med. J.*, 15, 103.

CONSTIPATION

See also B.E.M.P., Vol. III, p. 376; and Surveys and Abstracts 1939, p. 50.

Pathogenesis*Experimentally induced constipation*

J. Schwartzman and I. Weinstock studied the effect of constipation in 32 normal children. This was induced by giving them large doses of kaolin in aluminium hydroxide suspension. No significant harmful effects were noted as the result of the constipation, the children's actions at play, meal-times, and bedtime showing no deviation from normal. Blood pressures were unchanged, and there was a normal gain in weight. Laboratory investigation of the blood and urine did not show any significant alteration. Constipation as such should therefore not be considered a cause for alarm and hasty action. If accompanied by abnormalities, it should be considered as the effect rather than the cause of the condition.

Treatment*Unprepared bran*

F. P. Weber regrets that 'All-Bran', consisting almost entirely of cellulose and not a food as it cannot be absorbed, has been classed with 'luxury breakfast foods', and will no longer be obtainable when the present supply is exhausted. It is, as far as he is aware, the only properly prepared bran available in Great Britain, and this will entail hardship to many otherwise constipated subjects. How far ordinary bran, as given to animals, can be used for the same purpose he is at present unable to say. T. L. Cleave describes his method, employed for 10 years in the Royal Navy, of giving natural unprepared bran. It was always successful provided that the dose was maintained at an adequate level. The dosage varied with (1) the individual and with (2) the amount of cellulose in the food, for example, the Eskimo takes hardly any cellulose, whereas the African native consumes a vast quantity. In practice the dose varies from 1 teaspoonful to 2 tablespoonfuls before each meal; but the large dose is seldom required except in bed patients. But it is essential to start with the larger dose and then reduce it. There is said not to be any risk of infection with actinomycosis.

Cleave, T. L. (1941) *Brit. med. J.*, **1**, 461.

Schwartzman, J., and Weinstock, I. (1941) *Arch. Pediat.*, **58**, 251.

Weber, F. P. (1941) *Brit. med. J.*, **1**, 252.

CONTRACEPTION

See also B.E.M.P., Vol. III, p. 385; Cumulative Supplement, Key No. 258; and p. 102 of this volume.

Methods of Contraception*Spermicidal preparations*

Jellies.—Following a previous work of 10 years ago on the efficacy of jelly contraceptives using 2 per cent lactic acid jelly with chinosol, I. F. Stein and M. R. Cohen made further observations on 310 women, the latter being all referred to them by doctors. They were instructed in the use of a jelly contraceptive alone applied directly to the cervix by a special applicator. Its efficacy was measured by comparison of the number of pregnancies with the number of years of exposure to pregnancy risk. Expressed as a percentage, 87 per cent reduction in fertility was obtained compared with 76 per cent reported by others for the jelly and diaphragm method. Forty-seven pregnancies occurred, of which 20 represented true failures, in 18 the patient had been inconstant in the use of jelly, 3 were deliberate, 2 were due to reliance on condom protection, and in 1 the patient was judged incompetent. The jelly is considered relatively safe, acceptable, non-irritant. It is suggested that several alternative methods of contraception should be taught at clinics including the jelly-alone method.

The 'safe period'

S. Fleck, E. F. Snedeker, and J. Rock, in a discussion on the contraceptive safe period, consider that the 16th to 12th days inclusive before the first day of the next menstruation constitute the period during which ovulation occurs. An admittedly generous allowance of 3 days before and after this period is made for viability of spermatozoa and susceptibility of ova respectively. The postulated fertile period therefore extends from and including the 19th day before the earliest menstruation up to and including the 9th day before the latest likely menstruation.

Fleck, S., Snedeker, E. F., and Rock, J. (1940) *New Engl. J. Med.*, **223**, 1005.

Stein, I. F., and Cohen, M. R. (1941) *Amer. J. Obstet. Gynec.*, **41**, 850.

CONVULSIONS IN INFANCY AND CHILDHOOD

See also B.E.M.P., Vol. III, p. 406; and Surveys and Abstracts 1939, p. 291; 1940, p. 253.

Treatment*Treatment of underlying causes*

Sodium diphenyl hydantoinate.—W. A. Hawke employed sodium diphenyl hydantoinate (dilatantin sodium) in 25 cases of convulsions in children. In 4 cases the convulsions were due to cerebral agenesis, in 2 to cerebral birth injuries, in 1 to encephalitis, in 1 to cerebrospinal syphilis, and in 17 they were idiopathic. The results were observed over a period of 6 months. The dosage was 0.1 gramme 3 times a day for children over 6 years of age, and 0.05 gramme 3 times a day for children under 6. Mild toxic reactions were observed in 36 per cent of cases. The drug alone, or in combination with phenobarbitone, was able to control the symptoms

in 18 cases (72 per cent) as compared with 10 (40 per cent) controlled by previous forms of therapy.

Hawke, W. A. (1940) *Canad. med. Ass. J.*, **43**, 157.

CORNEA, INJURIES AND DISEASES

See also B.E.M.P., Vol. III, p. 424; Cumulative Supplement, Key No. 260; and Surveys and Abstracts 1939, pp. 128 and 292; 1940, p. 253.

Ulcers

Treatment

Hypopyon corneal ulcer treated by sulphonamides.—I. L. Johnstone reports on the treatment of hypopyon ulcers of the cornea with a sulphonamide. Forty-one patients were treated. Sulphapyridine drops were used in a 0.07 per cent solution in saline, isotonic with the lachrymal secretion. The results were better than those obtained by previous methods. Recovery was quicker and the corneal scars were less dense. Several recurring ulcers already treated by other methods were finally cured. Three ulcers with purulent regurgitation were healed with sulphapyridine powder. Subconjunctival injections of soluseptasine (10 per cent) were given in a few cases in which there was not any discharge. The following routine is suggested: (1) a smear and culture to be made; (2) atropine and cautery (the possibility of omitting the latter needs investigation); (3) subconjunctival injections of two or three depots of soluseptasine or sulphapyridine; (4) an appropriate sulphonamide powder according to the organisms present. Dusting is preceded by one drop of 1 per cent decicain (butethanol).

Intravenous injections of ascorbic acid.—T. K. Lyle and D. W. McLean find that the intravenous injection of ascorbic acid is of value in certain corneal conditions, particularly ulceration, superficial keratitis, and chronic corneal opacities. In most cases the improvement effected was extraordinary. In the cases observed there was not any obvious general vitamin C deficiency. Ascorbic acid does not seem to be effective in iritis. The dosage employed was 500 milligrams daily until active inflammation subsided, followed by 250 milligrams daily by mouth.

Symptomatic Affections

Herpes zoster

Convalescent blood.—T. Gundersen reports the results obtained from the use of convalescent blood in the treatment of herpes zoster ophthalmicus. If between 250 and 450 cubic centimetres of blood are given before ocular infection is well established, good results may be expected. In cases responding favourably to this treatment, no new corneal infiltrations develop, and those already present when the transfusions are given show some absorption; the aqueous clears, and there is lessening of the degree of pain.

Gundersen, T. (1940) *Arch. Ophthalm., N.Y.*, **24**, 132.

Johnstone, I. L. (1941) *Brit. med. J.*, **1**, 887.

Lyle, T. K., and McLean, D. W. (1941) *Brit. J. Ophthalm.*, **25**, 286.

CORNS AND BUNIONS

See also B.E.M.P., Vol. III, p. 433; and Surveys and Abstracts 1939, p. 294.

Corns

Treatment

Soft corns.—For the treatment of soft corns, which generally occur between the fourth and fifth toes, H. B. Macey recommends removal of the prominent portion of the phalanx of either the 5th or the 4th toe. Since the callus is generally situated over the prominent base of the proximal phalanx of the 4th toe, it appears to be more logical to excise this prominence than that of the 5th toe. It is important that the prominence should be removed so cleanly and smoothly that sharp spicules which would produce further symptoms do not remain.

Bunions

Treatment

R. T. McElvenny and F. R. Thompson employed simple exostosectomy for the relief of bunion pain in 100 cases; of these cases 77 were completely relieved of pain and discomfort, and 11 had vague aches and pains about the 1st metatarso-phalangeal joints which suggested arthritis. The results for the remaining 12 patients were disappointing, the cause of the pain and disability after operation being due either to wrong selection of the patient or to faulty operative technique. The authors conclude that patients most suitable for operation should be those primarily interested in the relief of bunion pain and not in the correction of the deformity, the circulation in the feet should be adequate, sesamoiditis should be absent, the great-toe motion at the first metatarso-phalangeal joint should be free and painless, and the hallux valgus should be less than 50 degrees when estimated by the angle which the great toe makes with the metatarsal shaft.

McElvenny, R. T., and Thompson, F. R. (1941) *J. Bone Jt Surg.*, **22**, 942.

Macey, H. B. (1940) *Proc. Mayo Clin.*, **15**, 549.

CORONERS AND INQUESTS

See also B.E.M.P., Vol. III, p. 437; and Cumulative Supplement, Key No. 264.

The Coroner*Appointment and qualifications*

Fees at inquests.—J. Taylor reviews in a Harveian Lecture the relations of the coroner, the doctor, and the public. In 1934 there were 534 coronerships in England and Wales, filled by 309 coroners. Of these 268 were barristers or solicitors, 37 were medical practitioners, and 4, survivors of the old order, had no such qualifications. A few, about 15, held both legal and medical qualifications. Of all these only 13 were whole-time coroners; this means that the great majority were solicitors functioning as coroners as a side line. It therefore sometimes happens that coroners act in their professional capacity as solicitors in matters which they have investigated as coroners, and this situation is likely to cause criticism. A medical man may also be placed in a similar invidious position. It was formerly the custom for the necropsy to be performed by the practitioner who reported the death. Now many coroners have the necropsy performed by a pathologist. At first this caused some dissatisfaction, on the grounds, apparently, that a fee was paid for the necropsy, which sometimes figured among the assets of a practice when for sale. It was argued that all practitioners are allowed to perform necropsies or capital operations. In London and in larger cities there is not any difficulty in getting the services of a pathologist, but in country districts it is otherwise. The distances to be covered by the pathologist are greater, but the fee is the same: the country mortuaries are often very primitive, many being without running water. The obvious remedy would be to move the body to the nearest suitable mortuary, were it not for the somewhat cumbersome procedure entailed when a body is taken from the district of one coroner to that of another. But when the smaller districts are merged into the larger, this difficulty will be much reduced. Some coroners have tried to avoid payment for medical evidence, the reason usually having been that the practitioner gave evidence in order to clear himself of criticism. But whatever the reason for his attendance the doctor is entitled to his statutory fee. One coroner paid fees even to well-known abortionists who, with his help, were on their way to the Old Bailey.

Taylor, J. (1941) *Med. Pr.*, **205**, 433.

CRANIAL NERVE AFFECTIONS

See also B.E.M.P., Vol. III, p. 470; and Surveys and Abstracts 1939, pp. 86 and 294; 1940, p. 255.

The Eighth Nerve*Tinnitus aurium*

Vascular origin.—J. C. Donnelly reports a case of objective tinnitus aurium of the vascular type in a woman aged 31. The condition presumably arose from an arteriovenous angioma. The most striking clinical feature was the immediate cessation of the noise when light pressure was applied to the internal jugular vein. Certain rotary movements of the head distinctly altered the bruit. Exercise at once exaggerated the rate and intensity of the murmur. Change of posture from a sitting to a reclining position increased the intensity. Closure of the auditory canal at once magnified the noise heard by the patient. On deep inspiration the bruit was more audible objectively.

Donnelly, J. C. (1940) *Arch. Otolaryng., Chicago*, **32**, 1054.

CROHN'S DISEASE

See also B.E.M.P., Vol. III, p. 508; Cumulative Supplement, Key No. 277; and Surveys and Abstracts 1939, pp. 49 and 294.

Clinical Picture

W. L. Graham adds 35 new cases to the 413 cases of regional ileitis or Crohn's disease already reported. In the 35 cases 65.6 per cent were males and 35.4 females; the average age was 27 years, 7 being in the decade 1 to 10, and 9 in the second decade. One case of hypertrophic tuberculosis was included in the 35. Operation was performed in 28 cases. The terminal ileum alone was affected in all the cases except one; in this instance an area of about 5 inches in the middle of the jejunum was involved. The obscure aetiology is discussed; Graham noticed that in his cases involving the terminal ileum only, the part of intestine attacked is that supplied with blood by the ileal branch of the ileocolic vessels; it is suggested that the changes are the result of lymphatic obstruction due to vascular obstruction. No fistula was reported in the author's 35 cases, in which 20 were diagnosed before operation as acute appendicitis. In 1 case fatal peritonitis and appendicitis occurred. Specific treatment with sulphanilamide or sulphapyridine was tried in 15 cases but without any obvious benefit.

Radiology

G. Friedlaender reviews present knowledge of regional ileitis described in 1932 by Crohn, Ginzburg, and Oppenheimer, refers to isolated earlier cases, including one in 1813, and quotes Schapiro's collection of 462 cases (56.5 per cent males; 43.5 females). He insists that X-ray examination is of paramount importance, because it is the only method, apart from laparotomy, of establishing the correct diagnosis with certainty. The signs, symptoms, and clinical course cannot do more than arouse a suspicion of the true diagnosis. In acute cases of regional ileitis patients are very seldom X-rayed, as such states are almost invariably regarded as acute appendicitis and operated upon at once. Nearly all the cases of regional

ileitis examined radiologically belong to the later stages in which there is absence of the normal mucosa pattern, due to swelling and ulceration of the mucosa, much irregularity of the outline, and narrowing and rigidity of the affected part. A constant filling defect is present, and the parts involved appear as a narrow, distorted linear shadow without peristalsis, resembling a twisted cord or piece of string in knots. The barium meal should be tried first and the meal followed down every half-hour to the caecum. The administration of a barium enema has also been recommended, but it may be attended by several drawbacks.

Metabolism

W. R. Todd, M. Dittebrandt, J. R. Montague, and E. S. West report their metabolic investigations on a man with regional ileitis who, as a result of 5 resections, had only 3 feet of small intestine. It was found, during 3 separate periods of study, that carbohydrates were utilized normally, and that proteins were not as well absorbed, being 76 per cent, 75 per cent, and 69 per cent respectively for 3 periods. More calcium was lost when larger amounts of fats, chiefly as fatty acids, were excreted in the faeces. Phosphorus excretion tended to correspond with that of calcium. Tetany was obviated only by a very high calcium and vitamin D (calciferol) intake, and was controlled more easily with a high-carbohydrate, low-fat intake.

Friedlaender, G. (1941) *Brit. J. Radiol.*, **14**, 164.

Graham, W. L. (1941) *Canad. med. Ass. J.*, **44**, 168.

Schapiro, R. (1939) *Amer. J. med. Sci.*, **198**, 269.

Todd, W. R., Dittebrandt, M., Montague, J. R., and West, E. S. (1940) *Amer. J. digest. Dis.*, **7**, 295.

CYSTICERCOSIS

See also B.E.M.P., Vol. III, p. 523; and Surveys and Abstracts 1940, p. 255.

Clinical Picture

Cerebral involvement

Difficulty of radiological detection.—W. P. MacArthur further emphasizes the difficulty of the radiological recognition of *Cysticercus cellulosae* cysts in the brain, by the record of a man who gave a history of head injury while in the Army and was examined in a Civil hospital by encephalography and other scientific measures, and firmly diagnosed as traumatic epilepsy. These diagnostic methods did not reveal the presence of the 50 cysticerci which at the necropsy 4 years later were counted in the brain. Intracerebral cysts usually do not die and calcify, and therefore radiological examination is likely to be negative.

Development of Cysticercus Cellulosae in Man

Incidence and detection

In an article on *Cysticercus cellulosae*, its radiographic detection in the musculature and the central nervous system, J. F. Brailsford summarizes his observations on this subject for 20 years. This infestation seldom arises in Great Britain: all the cases he has seen have been in soldiers after service abroad, chiefly in India, and its incidence in Europe has fallen with the progress of public hygiene. It is very rare for a patient with cysticercosis to give a history of having carried a tapeworm. There is a latent period of some years between the date of ingestion of the ova and the appearance of painless subcutaneous nodules. The ingestion of ova is not as a rule attended, as it is in trichinosis, by signs of gastro-intestinal irritation. The painless nodules, of which in one case 558 calcified cysts were counted, if periodically examined for a year or so may show enlargement followed by diminution in size. Radiological detection of nodules is not possible until calcification has taken place, so cysts with living parasites can only be established after surgical excision. After 4 or 5 years the contents of the cysts undergo coagulation necrosis and become turgid, translucent, and eventually opaque, and the author believes that calcium salts are first deposited in the contents, and not, as has been stated, in the walls, of the cysts. It is suggested that patients with living cysts should be given drugs, such as quinine, mercury, or sulphapyridine, which would probably inhibit the development of, or kill, the embryos, before attaining the stage at which their presence produces cerebral or other serious symptoms. The process of degeneration and calcification of the contents of the parasitic cysts does not occur so readily in the brain as in the muscles.

Brailsford, J. F. (1941) *Brit. J. Radiol.*, **14**, 79.

MacArthur, W. P. (1941) *Brit. med. J.*, **1**, 492.

DARIER'S DISEASE

See also B.E.M.P., Vol. III, p. 544; and Cumulative Supplement, Key No. 282.

Treatment

Vitamin A

S. M. Peck, L. Chargin, and H. Sobotka report an investigation on vitamin A therapy in 4 cases of keratosis follicularis (Darier's disease). All 4 patients, while on a normal vitamin A diet, showed a decided decrease in the vitamin A content of the blood serum. The carotene content of the blood was within normal limits. In 2 cases good correlation was obtained between the result of a dark-adaptation test and the vitamin A deficiency, as evidenced by

the findings in the serum. A dose of 200,000 U.S.P. units of vitamin A by mouth daily caused a gradual disappearance of the eruption.

Peck, S. M., Chargin, L., and Sobotka, H. (1941) *Arch. Derm. Syph., N.Y.*, 43, 223.

DEAFNESS

See also B.E.M.P., Vol. III, p. 555; Cumulative Supplement, Key No. 284; Surveys and Abstracts 1939, pp. 87, 100, and 296; 1940, p. 255; and p. 52 of this volume.

Types of Deafness

Psychological reactions

H. Frey discusses the psychological aspects of deafness by distinguishing between congenital deaf-mutes and 'deafened' people. Mental anomalies in the first category are often due to other factors accompanying deafness, such as abnormalities of the nervous system; this may account for the high rate of mental deficiency amongst deaf-mutes. The deaf often have an exaggerated conception of the extent of their deafness and its handicaps, which fosters a sense of organic inferiority. That deafness need not impair mental well-being is shown by the number of mentally normal and happily occupied deaf persons. The cure for this neurotic depression lies in psychic treatment to restore mental energy. A. B. Stokes maintains that the same general paths of response appear in all organic disabilities which cause social hardships, but that certain defects may release behaviour responses inherent in the personality, especially when the defect causes particular hardship for that person; for example, normal anxiety may become florid hypochondriasis under stress of deafness, and paranoia often arises in deaf people with slight paranoid tendencies. I. R. Ewing classifies reactions to deafness under four heads: capacity to hear what is said, to talk intelligibly, to think, and to be employed. Four cases illustrating these categories, are described. Deafness in children is a more acute problem, because they have not been able to complete the development of normal functions before the onset of deafness.

Diagnosis

Otosclerosis

V. Nasiell points out the difficulty in the differentiation between the symptoms of otosclerosis and those of an adhesive process. Since artificial conduction of sound can equally well be obtained in ankylosis of the stapes in both conditions, the similarity is not of any practical importance. Meyer's new therapeutic technique of drawing off cerebrospinal fluid is based on the doubtful assumption that decompression of the endolymph improves hearing. This method was tried by the author on 7 patients and was successful only in one case; this success is attributed to rest and sedatives. No conclusive evidence is yet available of a definite connexion between otosclerosis and endocrine activity, although otosclerosis has some connexion with pregnancy. Attempts to set up a sound fistula in the labyrinth have not yet been successful, because a satisfactory mechanico-acoustic sound conduction has never been achieved.

Treatment

Prostigmin methylsulphate

M. S. Ersner, I. A. Rush, and D. Myers report the results obtained with prostigmin methylsulphate in 59 cases of deafness and tinnitus aurium. The dosage was 1 cubic centimetre (0.5 milligram) of a 1 in 2,000 sterile solution of the drug, hypodermically, daily, 3 times weekly, or on alternate days. Some patients also received the drug by mouth. A minimum of 35 injections to each patient was given. Of the 59 patients, 26 (44 per cent) failed to show any benefit, 4 (6.7 per cent) said that some improvement had occurred, but there was no audiometric evidence to support this, 18 (30.5 per cent) stated that there was a transitory improvement, and 8 (13.5 per cent) had audiometric evidence of an 8 to 10 decibel improvement which was transitory. Three patients (5 per cent) had to abandon the treatment owing to a severe anginal syndrome.

Prostigmin

Chronic deafness.—K. M. Houser, E. H. Campbell, and H. Schluederberg employed prostigmin, as recommended by Davis and Rommel (1939), in a series of 56 carefully tested and controlled cases of chronic deafness. Treatment consisted of the hypodermic injection of 1 cubic centimetre of a 1 in 2,000 dilution of prostigmin methylsulphate, and, in addition, during the first 6 weeks of treatment the oral administration of 15 milligrams of prostigmin bromide. Of the whole series of cases only 2 patients (3.5 per cent) stated that they experienced any practical improvement in hearing; 7 felt that they had some relief of tinnitus, 3 were doubtful, and 46 definitely showed no improvement. No patient completely lost the tinnitus. The authors conclude that prostigmin is of little, if any, value in the treatment of deafness and tinnitus.

Round-window grafts

W. Hughson reports that in 60 per cent of 36 cases of deafness treated by means of round-window grafts, there was a subjective improvement in hearing. A statistical analysis of all the cases, whether favourable or unfavourable, in the light of four years' experience, showed that the trend is toward an improvement in hearing.

Davis, T. C., and Rommel, J. C. (1939) *Arch. Otolaryng., Chicago*, 29, 751.

- Ersner, M. S., Rush, I. A., and Myers, D. (1941) *Arch. Otolaryng., Chicago*, **33**, 193.
 Ewing, I. R. (1941) *Proc. R. Soc. Med.*, **34**, 315.
 Frey, H. (1941) *Proc. R. Soc. Med.*, **34**, 309.
 Houser, K. M., Campbell, E. H., and Schluederberg, H. (1940) *J. Amer. med. Ass.*, **115**, 994.
 Hughson, W. (1940) *Arch. Otolaryng., Chicago*, **32**, 611.
 Nasiell, V. (1941) *Arch. Otolaryng., Chicago*, **33**, 916.
 Stokes, A. B. (1941) *Proc. R. Soc. Med.*, **34**, 312.

DENTAL SEPSIS IN RELATION TO SYSTEMIC DISEASE

See also B.E.M.P., Vol. III, p. 596; Cumulative Supplement, Key No. 288; and Surveys and Abstracts 1939, p. 298; 1940, p. 256.

Dental Sepsis in Adults

Treatment

Short-wave therapy.—D. Kobak states that gingivitis and associated dental conditions may be effectively controlled by short-wave therapy. This treatment gives early relief of pain, soreness, and other symptoms. The best electrodes are of the air-spaced type. Of 64 patients treated 28 had gingivitis, 14 had signs of suppuration and loosening of the teeth, 6 had localized but considerable swelling of the gums on the labial and lingual sides, 5 had dry sockets, and 11 had post-extraction pain and bleeding. Of the patients with gingivitis, more than 78 per cent became free from symptoms, and of those with incipient paradentosis, 72 per cent became free from symptoms. All patients with granuloma, dry socket, or post-extraction pain obtained complete relief.

Conditions Associated with Dental Sepsis

Complications after extraction of teeth

Neurological complications.—B. J. Alpers reports 3 cases of neurological complications after the extraction of teeth. Complications which have been observed are blood-stream infections, metastatic encephalitis without blood-stream infection, brain abscess, meningitis, cavernous sinus thrombosis, neuro-retinitis, and degenerative conditions. There appears to be no relation between the location of the extracted teeth and the subsequent complications in so far as upper and lower teeth are concerned.

Alpers, B. J. (1940) *J. nerv. ment. Dis.*, **92**, 752.

Kobak, D. (1941) *Arch. phys. Ther.*, **22**, 282.

DENTITION

See also B.E.M.P., Vol. III, p. 603; and Surveys and Abstracts 1939, p. 299.

Abnormal Dentition

Hutchinson's teeth in non-syphilitics

L. Kerschbaumer reports four cases of typical Hutchinson's teeth in patients free from congenital syphilis. Two of the patients were schizophrenics, one was an epileptic with psychotic symptoms, and the fourth was a psychoneurotic. All four patients came from a definitely 'tainted' stock in which alcoholism, neurosis, tuberculosis, and psychoses were present. The author states that the dental changes in these cases were probably due to the influence of a pathologically altered metabolism.

Kerschbaumer, L. (1941) *J. nerv. ment. Dis.*, **93**, 613.

DERMATITIS DUE TO INJURY AND POISONING INCLUDING FEIGNED ERUPTIONS

See also B.E.M.P., Vol. III, p. 609; and Surveys and Abstracts 1939, p. 299; 1940, p. 257.

Externally Applied Agencies: Direct Exposure

Radio-dermatitis

Surgical treatment of irradiation dermatitis.—R. K. Ghormley reviews the 97 patients attending for X-ray and radium dermatitis at the Mayo Clinic. Of these, 20 had become epitheliomatous, and were divided according to Broders's histological classification, into grade 1, five cases; grade 2, six cases; grade 3, eight cases; and grade 4, one case. This form of dermatitis is potentially malignant, and although malignant change develops in some only of the patients, the incidence is so high as to make adequate treatment imperative in all cases, particularly those with ulceration. The best treatment is wide excision followed by some form of skin grafting, especially free split grafts or thick Thiersch grafts, the Paget dermatome for cutting these grafts being most useful. In some parts of the body, such as the heel and sometimes the sole, a pedicle graft may be necessary. Amputation was performed in fifteen cases, only one so far proving fatal. Eleven were finger cases, two through the thigh, and two through the toes. Seven of these amputations were for squamous-celled carcinoma.

Toxic dermatitis

Irritating plants.—J. T. Martin and K. H. C. Hester carried out patch tests of powdered and dissected pyrethrum flowers, in an investigation of dermatitis caused by insecticides containing pyrethrum. The causal agent, or agents, of the dermatitis appear to be concentrated in the lower parts of the flower-head. Pollen alone gave only a slight reaction. A colour-

less extract, obtained by petroleum ether extraction of the flowers mixed with charcoal, gave an intense reaction. The pyrethrins were devoid of dermatitis-producing properties, but the volatile oil was highly active.

Poison ivy.—B. Shelmire states that 10 per cent perborate ointment gives little protection against the dermatitis due to poison ivy. The amount of protection appears to be directly proportional to the thickness of the powdery film left after evaporation of the water of the vanishing cream. That this partial protection is entirely mechanical, and not due to detoxification of the oil by the perborate, is indicated by the fact that the oleoresin of poison ivy deteriorates slowly, if at all, in the presence of liberal amounts of free oxygen, and because inert zinc oxide or calamine in vanishing cream affords equal protection against poison ivy dermatitis.

R. J. Reuter and S. J. White report the results of tests of the susceptibility of 23 subjects to poison-ivy dermatitis. Twenty gave a positive reaction, and 15 of these reacted to the first exposure. The shortest period of latency was one day, the longest 18 days, and the average 6 days. The duration of the reaction varied from 2 to 21 days. There were not any apparent variations according to sex, race, or site of inoculation.

According to L. Zisserman, the degree of susceptibility to poison ivy dermatitis reaches a high level in boys from 12 to 16, but decreases rapidly thereafter. There is not any relation between sensitivity to poison ivy and such physical characteristics as weight or colour of hair, nor is there any relation between sensitivity to poison ivy and sensitivity to sunlight, or between susceptibility to the plant and the commoner forms of allergy such as hay fever, asthma, eczema, or urticaria.

S. H. Silvers reports a case of stomatitis venenata and dermatitis of the anus resulting from chewing poison ivy leaves. The patient, a woman aged 38, with a known sensitivity to poison ivy, chewed the leaves on the advice of a medical practitioner in the belief that it would benefit her skin eruption. Two days after the start of this treatment her lips became swollen, and an eruption appeared in the mouth and on the hands. After another 2 days, the anal region became sore and itchy. There were not any gastro-intestinal symptoms.

Iroko wood.—J. M. Davidson describes the toxic effects due to contact with an African wood, iroko, in a carpenter's shop. The dust from this timber was moister than that generally associated with more seasoned wood, and tended therefore to adhere more readily to the skin. Of more than 50 men exposed to this wood, nearly all complained of irritation of exposed skin surfaces, 9 of more severe symptoms, such as itching of the exposed skin surfaces; some suffered from irritation of covered parts, especially the neck, axillae, antecubital fossae, genitalia, and backs of the knees, acute corzya, a sensation of constriction of the chest, retrosternal compression, dry cough, and dyspnoea.

Carrots.—H. R. Vickers reports 7 cases of dermatitis due to the handling of carrots in a large cannery. In 5 of the cases the rash remained localized to the hands, and in 2 the forearms, face, and neck were affected. The rash rapidly faded when the patients stopped work and applied a soothing lotion. Of 205 normal individuals tested, 32 were susceptible to carrot. Dermatitis was produced after contact for periods up to 3 days.

Gentian violet.—C. K. Good reports a case of ulcerative reaction after the use of gentian violet in the treatment of impetigo. Ulceration was accompanied by swelling and oedema of the cheek and small vesicle formation. There was slight glandular enlargement on the affected side.

Ethyl mercury phosphate.—F. J. Vintinner reports 42 cases of dermatitis venenata from the use of an aqueous solution of ethyl mercury phosphate. These cases occurred among workers employed in a wood-preserving process in several lumber mills. The constant contact of the hands and forearms with the solution caused a burning sensation, swelling, and blebs. The condition causes disability lasting from 5 to 30 days.

Lip-stick cheilitis.—M. B. Sulzberger and R. Hecht present further evidence that patients with irritation of the lips due to lip-stick (lip-stick cheilitis) are often allergically sensitive to the commercial dyes used in cosmetics. The purification of a commercial brand of tetrabromofluorescein abolished, or materially reduced, its capacity to elicit allergic reactions when applied as patch tests. The purification of commercial lithol red and of commercial dibromofluorescein, also reduced their capacity to produce allergic reactions when applied as patch tests.

Due to nail polish.—J. F. Burgess reports 10 cases of nail polish dermatitis; all of the patients gave a history of repeated violent or mild exacerbations every few days of a generally not entirely disappearing patchy eruption of the face and neck. The eruption was not uniformly symmetrical, but was often unilateral. The areas most commonly affected were about one or both eyes, around the mouth, the sides of the neck, and the supra-clavicular regions. In one case pruritus ani, due to repeated contact with nail polish was found. In one case only was there an eczema of the fingers. Nail polish thus rarely affects the fingers, but some more or less distant area. Patch tests in these cases were repeatedly positive.

Sulphonated oil as a detergent in dermatitis venenata.—C. G. Lane and I. H. Blank report on the use of sulphonated oil as a detergent in 279 cases of skin diseases; most of the patients showed lesions of the hand and were diagnosed as contact dermatitis, dermatitis venenata, or eczema. Whilst using the oil about 80 per cent of the patients showed improvement of the condition, and in only 8 per cent did it become worse. Less than 1 per cent of 350 patients

gave a positive reaction to patch tests. Almost all patients with dermatoses, for which soap is contra-indicated, such as atopic dermatitis, contact dermatitis, and seborrhoeic dermatitis, can maintain satisfactory hygiene by the use of sulphonated oil.

- Burgess, J. F. (1940) *Canad. med. Ass. J.*, **43**, 544.
 Davidson, J. M. (1941) *Lancet*, **1**, 38.
 Ghormley, R. K. (1941) *Proc. Mayo Clin.*, **16**, 69.
 Good, C. K. (1941) *Arch. Derm. Syph., N.Y.*, **43**, 704.
 Lane, C. G., and Blank, I. H. (1941) *Arch. Derm. Syph., N.Y.*, **43**, 435.
 Martin, J. T., and Hester, K. H. C. (1941) *Brit. J. Derm.*, **53**, 127.
 Reuter, R. J., and White, S. J. (1941) *New Engl. J. Med.*, **224**, 460.
 Shelmire, B. (1941) *J. Amer. med. Ass.*, **116**, 681.
 Silvers, S. H. (1941) *J. Amer. med. Ass.*, **116**, 2257.
 Sulzberger, M. B., and Hecht, R. (1941) *J. Allergy*, **12**, 129.
 Vickers, H. R. (1941) *Brit. J. Derm.*, **53**, 52.
 Vintinner, F. J. (1940) *J. industr. Hyg.*, **22**, 297.
 Zisserman, L. (1940) *J. Allergy*, **11**, 600.

DERMATITIS EXFOLIATIVA

See also B.E.M.P., Vol. III, p. 619; and Surveys and Abstracts 1940, p. 260.

Aetiology

Phenobarbitone

Fatal case.—D. L. Sexton, G. M. Pike, and A. Nielson report a fatal case of exfoliative dermatitis due to phenobarbitone. A man aged 39 years, was admitted with peptic ulcer, and was first given phenobarbitone subcutaneously, later by mouth, receiving in all 42 grains of the drug during 13 days. On the appearance of a rash, the drug was stopped, but the exfoliation continued, and the patient died.

Naphthalene

S. J. Fanburg describes a case of exfoliative dermatitis due to naphthalene in a man of 43. The offending agent was a pair of trousers which for several months had been in a drawer with naphthalene moth flakes. The eruption closely resembled that of mycosis fungoides both clinically and histologically. The author suggests that a more careful allergic study should be made in proved as well as suspected cases of lymphoblastomas, especially those with a history of remissions while the patient is in hospital.

Fanburg, S. J. (1940) *Arch. Derm. Syph., N.Y.*, **42**, 53.

Sexton, D. L., Pike, G. M., and Nielson, A. (1941) *J. Amer. med. Ass.*, **116**, 700.

DERMATITIS HERPETIFORMIS

See also B.E.M.P., Vol. III, p. 627; and Surveys and Abstracts 1939, p. 300.

Clinical Picture

Sensitization to halogens and bacterial allergens

J. L. Callaway and T. H. Sternberg discuss the origin and treatment of dermatitis herpetiformis. Although it has been claimed that there is a close relation between this disease and pemphigus vulgaris, and on the other hand that a specific virus for dermatitis herpetiformis has been found, it appears that the cutaneous aspect of the disease is the result of specific sensitization to halogens and to bacterial allergens. A case is described to substantiate this argument. The patient had suffered from a pruritic vesicular and bullous eruption for 6 years without any benefit from treatment. Radiologically there was evidence of low grade bronchiectasis, and a pure culture of pneumococcus (Type VII) was obtained. The patient was hypersensitive to many bacterial allergens, bromides, iodides, to patch tests and to intracutaneous injections of the vaccine derived from the pneumococcus culture. Desensitization and healing of the lesions were obtained after the use of 0.1 cubic centimetre of the vaccine on alternate days rising to 1 cubic centimetre. Over-dosage and suspension of treatment brought about a temporary relapse. It is possible that the disease may be caused by a virus which is activated by an allergic factor. A study of the agglutinins and precipitins in such cases might produce significant results.

Callaway, J. L., and Sternberg, T. H. (1941) *Arch. Derm. Syph., N.Y.*, **43**, 956.

DERMOID CYSTS

See also B.E.M.P., Vol. III, p. 635; and Surveys and Abstracts 1940, p. 261.

Congenital

Of nasal septum

A. L. Juers reports a case of dermoid cyst present since childhood in the nasal septum in a patient aged 19. In most reported cases such a cyst has been in the upper portion of the nose, and has required an external operative approach. In this case the cyst was confined to the cartilaginous part of the septum, and the fistula opened between the two lower alar cartilages on the dorsum of the nose. The cyst was removed intranasally.

Juers, A. L. (1941) *Arch. Otolaryng., Chicago*, **33**, 851.

DIABETES INSIPIDUS

See also B.E.M.P., Vol. III, p. 639; Cumulative Supplement, Key No. 295; and Surveys and Abstracts 1939, p. 301; 1940, p. 261.

Treatment*Total thyroidectomy*

H. Blotner and E. C. Cutler describe the treatment of 3 patients with diabetes insipidus, by total thyroidectomy. In each case the disease had been present for some years before investigation, and its progress was observed for 5 years after operation. The first patient, a woman aged 66, had idiopathic diabetes insipidus accompanied by a high basal metabolic rate, high cholesterol and calcium blood contents. Thyroidectomy did not have any effect on the water balance, but reduced the calcium level and temporarily the basal metabolic rate. The two other patients had post-encephalitic diabetes insipidus accompanied by Parkinson's disease, both of which were somewhat alleviated by thyroidectomy. The intake and output of water increased again on administration of thyroid. That the action of thyroid is not due to its power of raising the basal metabolism is shown by the fact that when the latter was artificially raised by dinitrophenol the action of thyroid in restoring polyuria was diminished. Conversely when the basal metabolic rate was still low as a result of thyroidectomy, restoration by thyroid was effective. The failure of treatment in the first patient is ascribed to accessory thyroid tissue, because after thyroidectomy there was not any sign of myxoedema, and the basal metabolic rate was unchanged.

Pitressin tannate

Comparison with other posterior pituitary preparations.—J. A. Greene and L. E. January administered pitressin tannate in oil to 3 patients with diabetes insipidus, and to 3 cats with the experimentally produced disease. They compared the duration of effect and the efficacy of this method of treatment with that of other preparations of the posterior pituitary. The duration of the effect in cats was found to vary from 3 to 7 days, and in patients from 30 to 82 hours. The effect on the manifestations of the disease in the patients was equal to that of other preparations of the posterior pituitary, and there were not any disagreeable side-effects. The dosage employed in the case of the patients was 1 to 2 cubic centimetres of pitressin tannate in oil on alternate days.

Blotner, H., and Cutler, E. C. (1941) *J. Amer. med. Ass.*, **116**, 2739.

Greene, J. A., and January, L. E. (1940) *J. Amer. med. Ass.*, **115**, 1183.

DIABETES MELLITUS

See also B.E.M.P., Vol. III, p. 644; and Surveys and Abstracts 1939, pp. 67 and 301; 1940, p. 262.

Diabetes Mellitus*Aetiology*

Pituitary anti-diabetogenic principle.—R. D. Lawrence and F. G. Young, in observations on patients with diabetes mellitus rendered permanently diabetic by the administration for a short period of anterior pituitary extract, could not find any evidence to support Collip's claim that the oral administration of 'the primary alcoholic extract of pituitary tissue' exerts a profound 'anti-diabetogenic effect'.

H. P. Marks and F. G. Young investigated the pancreotrophic activity of different anterior pituitary preparations. Collip's primary neutral alcoholic extract of pituitary tissue was found not to be significantly pancreotrophic when administered to rats either subcutaneously or orally.

Clinical picture

Nephrotic syndrome with hypertension.—According to M. A. Simon, old patients with diabetes mellitus of long standing may present a nephrotic syndrome, characterized by massive oedema of nephrotic distribution, hypoproteinaemia, hypoalbuminaemia, lowering of the albumin-globulin ratio, and massive albuminuria. This is accompanied by hypertension and a variable degree of renal failure. The cases of 2 Jews, about 65 years of age, one male and one female, with systolic blood pressures of about 170 to 200 millimetres of mercury, are reviewed. Including these the number collected amounts to 21. The kidneys of the 2 patients were about the normal size; the capsules peeled off readily, exposing a finely granular surface. The cortex was somewhat diminished. The lesions were mainly in the glomeruli and were degenerative, not inflammatory or of ordinary glomerulo-nephritis. The fundamental change consists in the deposit in the glomeruli of a non-cellular, homogeneous, hyaline mass containing variable amounts of double refractile lipid between capillary loops of the glomeruli. This extra-cellular substance does not stain like amyloid though there is a resemblance in some other respects. Bowman's capsule is covered by similar material which is more fatty. All sections of the kidney show moderately advanced arteriolar change with the media containing lipohyaline material. The kidneys did not show the changes of nephrosis, and the medium-sized arteries did not contain the lipohyaline material.

Associated with tuberculosis.—R. M. McKean, G. C. Thosteson, and N. Brooks review the treatment of tuberculosis with associated diabetes mellitus during a period of 10 years. They found that the distribution of the type of tuberculous disease and average severity of diabetes mellitus remained about the same over that period. A marked increase in the use of collapse

therapy in general had occurred. From the metabolic standpoint, an increase in the carbohydrate allowance and a reduction of fat in the diets had been most apparent. Slightly more than 80 per cent of the patients required insulin, with an average of 42 units. The mortality in cases with associated diabetes mellitus and tuberculosis paralleled closely that of pulmonary tuberculosis alone.

Pellagra-like condition.—A. Rudy reports a case of deficiency disease in a man, aged 52, with diabetes mellitus. His condition was not unlike pellagra, with neurological, cutaneous, and gastro-intestinal manifestations simulating syphilis of the central nervous system and gastro-intestinal malignancy. There was definite improvement after the administration of vitamin B₁ parenterally and vitamin B complex orally.

Symmetrical peripheral neuropathy.—H. D. Fein, E. P. Ralli, and N. Jolliffe found that, of 422 ambulant diabetic patients, 9 (2.1 per cent) had a symmetrical peripheral neuropathy characteristic of the peripheral neuropathy in patients with a proved vitamin B₁ deficiency. In 8 of these cases treatment consisting of the daily administration of 10 milligrams of thiamin (aneurin) by mouth, without otherwise changing the regimen, effected a cure, and led to improvement in the ninth case.

Diagnosis

Wesselow and Griffiths' test.—J. G. Rushton and R. M. Wilder confirm in part the theory of De Wesselow and Griffiths that 2 types of diabetes mellitus could be distinguished by the presence in the blood of substances inhibitory to insulin. Rushton observed that the plasma of 6 out of 44 patients examined gave a positive response to De Wesselow and Griffiths' test. These 6 patients had diabetes mellitus. Their ages ranged from 9 to 53, and their insulin requirements from 0 to 90 units.

Treatment

Zinc protamine insulin.—E. Tolstoi and F. C. Weber, Jun., treated 84 patients with diabetes mellitus with one daily dose of zinc protamine insulin, varying from 10 to 60 units. No particular effort was made to maintain the urine free from sugar, and yet only 27 patients showed almost continuous glycosuria throughout the period of study (one year). The great majority of patients maintained their weight, and many gained weight. None presented any symptoms of diabetes mellitus, and only one showed mild acetonuria (rarely). Their food was not weighed. The incidence of infection was no greater in this series than in other patients. The authors consider that guiding principles for the satisfactory treatment of diabetes mellitus with zinc protamine insulin are the maintenance of weight, freedom from symptoms of diabetes, and absence of ketone bodies from the urine.

Zinc protamine insulin for diabetes with tuberculosis.—H. O. Mosenthal and M. F. Mark again report their experience of the use of zinc protamine insulin as an alternative to unmodified insulin in the treatment of diabetes mellitus accompanied by tuberculosis and point out the importance of controlling the diabetes before the tuberculosis can be successfully treated. The rigid conception of normality in the control of diabetes mellitus based on the absence of urine sugar and normal blood sugar is criticized. Elevation of blood sugar without glycosuria is even beneficial and loss of sugar by the urine has no adverse effects if it is not accompanied by nitrogen loss. This is the case when zinc protamine insulin is given. Persistent glycosuria may be disturbing, but it is less harmful than hypoglycaemia. There is an impression that ketonuria, diabetic coma, and gangrene of the lower extremities are less frequent when zinc protamine insulin is used. Formerly it was given only once in the day and without any rule that meals must be taken within a definite time limit. Two hundred and seventy-eight patients were observed. Regular insulin was given to 131 of them and zinc protamine insulin to 147 of them. The tuberculosis in the second group of patients had a more favourable clinical course than in those of the first group. Advance of the disease or a fatal termination occurred in 28.9 per cent of the second group of patients, and in 73.4 per cent of the first group of patients.

Evaluation of aneurin administration.—L. B. Owens, S. S. Rockwern, and E. G. Brown state that the usual diabetic dietaries contain adequate amounts of aneurin (thiamin) and riboflavin in relation to their total calorific value. The administration of large amounts of aneurin (thiamin) and riboflavin to well-controlled diabetics for many weeks does not reduce the insulin requirement or alter the severity of the diabetes. There does not seem to be any need for extra aneurin, except in diabetic neuritis. Dextrose tolerance regularly increases in diabetics as their state is controlled by diet and insulin. Many of the claims of benefit from vitamin therapy have been based on clinical testing before the disease had been brought under proper control by diet and insulin.

Ascorbic acid.—L. B. Owens, J. Wright, and Edna Brown gave ascorbic acid in doses of 300, 600, and 1,200 milligrammes daily to 16 patients with diabetes mellitus in various stages of vitamin C nutrition. No constant objective improvement or any change in the severity of the disease was observed. There was not any gain in weight or significant change in the insulin requirement. Although there is experimental evidence, which is quoted, that ascorbic acid has a beneficial effect on the normal or diabetic individual's power to metabolize glucose or store of glycogen, no practical benefit has resulted in its use in human diabetes mellitus in any dosage or for any length of time. There was, however, some subjective improvement consisting of increased strength and endurance in 9 of the 16 patients; the least improvement was observed in those who began with a poor state of vitamin C nutrition.

Insulin-quinine.—W. C. Cutting and G. B. Robson report that 7 out of 10 patients with mild or severe diabetes mellitus reacted beneficially when given varying doses of an insulin-quinine mixture by mouth. On the whole the effect was irregular and the undesirable effects of cinchonism were observed in about 50 per cent of the patients. The authors regard the results obtained as encouraging about the future possibilities of the discovery of more efficient and less objectionable agents than quinine for promoting gastro-intestinal absorption of insulin. At present the insulin-quinine mixture is not recommended for general clinical use.

Pre-operative procedure.—P. C. Eschweiler states that the usual pre-operative procedure of giving an infusion of 500 cubic centimetres of 10 per cent glucose 'covered' by 25 units of insulin in diabetes mellitus complicated by obstetrical or surgical conditions, often results in hypoglycaemic reactions. In order to determine whether all patients with diabetes mellitus can tolerate the same amount of insulin with an infusion of glucose, intravenous tolerance tests were given to 5 patients with diabetes mellitus of various severity and to 1 normal patient. It was found that insulin is not required to reduce the blood sugar values near to the fasting level after the intravenous administration of 500 cubic centimetres of 10 per cent glucose, as the blood sugars of the patients with diabetes mellitus reached blood sugar levels approximating to their usual fasting levels within 1½ to 2 hours. It was also shown that the milder the case of diabetes, the more nearly was approached the curve representing the non-diabetic patient. It may therefore be concluded that insulin should never be administered as a routine to 'cover' parenterally administered glucose in patients with diabetes mellitus. The diabetic status of the patients must be taken into consideration.

Diabetic Coma

Treatment

Warning symptoms.—L. Cole describes the occurrence, causes, symptoms, and treatment of diabetic coma in 24 young diabetic patients. Thirteen attacks of coma occurred, 6 of them in patients in whom there had not been any previous diagnosis of diabetes mellitus, and 7 of them during insulin treatment. In 9 patients the coma coincided with infection. The omission or reduction of the insulin dose during infection almost inevitably results in diabetic coma. It rarely occurs in an uninfected patient under insulin. Warning diabetic symptoms of coma are constant, but may not always be obvious and the coma may be the first indication of diabetes mellitus. Failure, however, to examine the urine in the face of the slightest suggestive symptoms may be disastrous. The warning symptoms are vomiting, abdominal pain, dehydration, alteration of breathing, sugar in the urine, a positive Gerhard test, increased blood sugar, and inability to take the routine diet. In this event insulin must not be stopped. An unusual case is described in which the patient showed only faintly positive reaction of Rothera and Gerhard tests at the onset of coma, and the main symptoms were nausea and vomiting, suspension of insulin being followed by a very severe attack of coma. Treatment should consist of insulin and glucose, fluids and normal saline, warmth and ephedrine, gastric lavage for vomiting, and enemas. The dose of insulin varies, but should be from 20 to 100 units, usually not less than 50. Suggestions are made for the prevention of coma, including the early diagnosis of diabetes mellitus and better teaching in the care of diabetics especially during infection.

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Collip, J. B. (1940) *Canad. med. Ass. J.*, **42**, 109.

Cutting, W. C., and Robson, G. B. (1941) *Endocrinology*, **28**, 375.

Eschweiler, P. C. (1940) *Surg. Gynec. Obstet.*, **71**, 141.

Fein, H. D., Ralli, E. P., and Jolliffe, N. (1940) *J. Amer. med. Ass.*, **115**, 1973.

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McKean, R. M., Thosteson, G. C., and Brooks, N. (1941) *Amer. Rev. Tuberc.*, **43**, 31.

Marks, H. P., and Young, F. G. (1940) *Lancet*, **2**, 710.

Mosenthal, H. O., and Mark, M. F. (1939) *J. Amer. med. Ass.*, **113**, 17.

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— Wright, J., and Brown, Edna (1941) *Amer. J. med. Sci.*, **201**, 636.

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Rushton, J. G., and Wilder, R. M. (1940) *Proc. Mayo Clin.*, **15**, 417.

Simon, M. A. (1940) *Canad. med. Ass. J.*, **43**, 425.

Tolstoi, E., and Weber, F. C., Jun. (1940) *Arch. intern. Med.*, **66**, 670.

De Wesselow, O. V. L., and Griffiths, W. J. (1936) *Lancet*, **1**, 991.

DIAPHRAGM DISEASES

See also B.E.M.P., Vol. III, p. 673; and Surveys and Abstracts 1939, p. 309; 1940, p. 268.

Abnormalities of the Diaphragm

Paroxysmal flutter

M. J. Goodman reports an extraordinary case of paroxysmal flutter of the diaphragm associated with severe precordial pain which led to the erroneous diagnosis of coronary

thrombosis. Spraying the intact skin overlying the phrenic nerve in the neck on the involved side with ethyl chloride promptly controlled both the pain and the flutter.

Goodman, M. J. (1941) *J. Amer. med. Ass.*, **116**, 1635.

DIARRHOEA

See also B.E.M.P., Vol. IV, p. 1; and Surveys and Abstracts 1940, p. 269.

Clinical Picture

Vitamin deficiency diseases

W. B. Bean and T. D. Spies found, in an area of endemic pellagra, beri-beri, and riboflavin deficiency, 100 individuals who acquired such syndromes as a complication of chronic diarrhoea; the latter disposes to deficiency syndromes by causing increased loss and decreased absorption of vitamins. When the diarrhoea is relieved, even without vitamin therapy, the secondary deficiencies generally respond. In these deficiency diseases due to chronic diarrhoea, parenteral injection of crystalline vitamins are essential, but do not take the place of a high protein, high caloric diet. In most cases the use of nicotinic acid, from 500 to 1,000 milligrams daily, thiamin hydrochloride (from 10 to 50 milligrams daily), and riboflavin (from 2 to 10 milligrams daily) relieves specific deficiencies.

Bean, W. B., and Spies, T. D. (1940) *J. Amer. med. Ass.*, **115**, 1078.

DIARRHOEA ASSOCIATED WITH FLAGELLATE INFECTION

See also B.E.M.P., Vol. IV, p. 12; Cumulative Supplement, Key No. 306; Surveys and Abstracts 1939, p. 310; 1940, p. 269; and p. 24 of this volume.

Giardia Intestinalis

Treatment

Atebrin dihydrochloride.—P. B. Nutter, Enid C. Rodaniche, and W. L. Palmer state that infection with *Giardia lamblia* is often present in patients with moderate or intermittent diarrhoea, with mild digestive symptoms, and without occult blood in the faeces. The symptoms often, but not invariably, disappear after the eradication of the parasite. In the authors' experience the diarrhoea invariably disappears. Atebrin dihydrochloride is a highly satisfactory drug for the treatment of giardiasis. The toxic effect of the drug is slight, and routine treatment can be established with safety.

Nutter, P. B., Rodaniche, Enid C., and Palmer, W. L. (1941) *J. Amer. med. Ass.*, **116**, 1631.

DIARRHOEA IN INFANCY AND CHILDHOOD

See also B.E.M.P., Vol. IV, p. 21; and Surveys and Abstracts 1939, p. 310; 1940, p. 270.

Pathology and Bacteriology

Biochemistry

Excretion of vitamin C.—A. F. Abt and C. J. Farmer report their observations on the excretion of vitamin C after oral administration to infants with diarrhoea. Previous work has shown that its rate of excretion in normal infants is low in spite of high oral intake and that after catharsis there is a sharp rise in the amount excreted. The vitamin C contents of the stools, urine, and blood plasma were determined in 3 infants with non-specific diarrhoea. After oral administration of vitamin C there was a sharp rise in faecal excretion, pointing to a failure in vitamin C absorption by the intestine, the blood plasma level and urine content remaining low. When stools began to form there was a decrease in faecal vitamin C content. In one patient this was accompanied by a rise in the plasma and urine levels. Although scurvy could not develop in short attacks of diarrhoea, the possibility of its occurrence in prolonged attacks should be considered. Moreover, when the plasma level of vitamin C is already at the minimum before the onset of scurvy, diarrhoea or dysentery may precipitate scurvy in adults as well as in infants, indicating the need of parenteral administration of ascorbic acid.

Treatment

Drugs

Sulphathiazole.—G. Taylor reports on the use of sulphathiazole in 13 cases of infantile diarrhoea. The initial dosage was 1 gramme per year of age up to a maximum of 3 grammes by mouth, followed by the same daily amount divided into 6 doses. The average time for the stools to reach four a day, of normal colour and consistency, was 3.2 days in the children given sulphathiazole, and 15.6 days in the control group. Of 14 controls, 2 patients died, whereas there were not any deaths among those treated by sulphathiazole.

E. V. Anderson reports the results of sulphathiazole in the treatment of 17 cases of infective diarrhoea and of 16 cases of non-infective diarrhoea in children. There were not any deaths, as compared with a mortality rate of 34.5 per cent in the infective cases and 13.5 per cent in non-infective cases under previous routine therapy. In the new procedure bismuth, paregoric, atropine or other medicaments were not used to check diarrhoea. The drug was administered orally (1–1.5 grains per pound of body weight) with an average duration of 4½ days for the treatment. The diarrhoea did not recur when the treatment was discontinued and no toxic symptoms, except for fever and rash in one patient, were seen. Skimmed milk or high carbohydrate, low-bulk diet was given and preliminary starvation was omitted. The

criterion of recovery in infective patients was three negative stools, and for non-infective patients, absence of blood, pus, and severe toxic symptoms.

Banana preparations

I. J. Wolman and R. L. Roddy, in a trial of banana and banana powder for 2 years, treated 97 infants and children with diarrhoea. A control group of 80 patients received one of several other recognized methods of therapy. Banana feeding was as effective a means of treating diarrhoea as the older and more usual feeding regimes. Banana preparations were well taken, and generally relieved hunger, tenesmus, and abdominal discomfort, and enabled the patients to pass semi-formed stools.

Abt, A. F., and Farmer, C. J. (1941) *J. Pediat.*, **18**, 756.

Anderson, E. V. (1941) *J. Pediat.*, **18**, 732.

Taylor, G. (1941) *J. Pediat.*, **18**, 469.

Wolman, I. J., and Roddy, R. L. (1940) *Amer. J. Dis. Child.*, **60**, 333.

DIETETIC DEFICIENCY DISEASES

See also B.E.M.P., Vol. IV, p. 51; Surveys and Abstracts 1939, p. 311; 1940, p. 271; and p. 5 of this volume.

Deficiency of Vitamin A

Treatment

Keratomalacia.—H. K. Goldberg and K. Schlivek report a case of keratomalacia due to vitamin A deficiency as a result of faulty absorption of vitamin A. The patient, a woman aged 23 years, was extremely emaciated, and with cutaneous ulceration. Marginal corneal ulcer arose which perforated with escape of the aqueous humour. Prolapse of the iris did not occur. She was given intramuscular injections of 100,000 units of vitamin A on 3 successive days. The eyes cleared remarkably. The anterior chamber reformed and, within 1 week, the corneal defect had filled in with scar tissue, and the vision had become normal.

Goldberg, H. K., and Schlivek, K. (1941) *Arch. Ophthalm.*, N.Y., **25**, 122.

DIPHTHERIA

See also B.E.M.P., Vol. IV, p. 72; Cumulative Supplement, Key No. 324; Surveys and Abstracts 1939, pp. 41, 74, and 312; 1940, p. 271; and pp. 4 and 66 of this volume.

Bacteriology and Pathology

Strains

Diffusing factor and substance B.—D. McClean reports that from examination of 50 strains of *C. diphtheriae*, he could not find any evidence of association between diffusing factor or hyaluronidase and substance B postulated by O'Meara to be present in toxic diphtheria filtrates. Only a small proportion of strains of *C. diphtheriae* of any type produced definite amounts of a diffusing factor. Saline extracts of those strains that produce this enzyme in broth culture show little or no diffusing activity. The capacity to form this enzyme is not confined to gravis strains; it can be detected in broth culture—with cultures of a few intermediate and mitis strains. The amount of this enzyme produced by any strain is very small compared with that found in cultures of organisms of the gas-gangrene group, streptococci, pneumococci, or staphylococci. Because of this, and the small proportion of strains from which the enzyme can be obtained at all, it is doubtful if an enzyme of this nature makes any material contribution to the symptom-complex of diphtheria.

Virulence test

Viability and air-borne infections.—W. E. Crosbie and H. D. Wright report isolation of virulent diphtheria bacilli in large numbers from floor dust in the neighbourhood of diphtheria patients. The bacilli may persist in a fully virulent form in such dust for at least 14 weeks *in vitro* and for 5 weeks on the floor. Disturbance of the dust allows the bacilli to pass into the air. Treatment of the floors with spindle oil reduces, and may entirely eliminate, air-borne contamination from this source.

Schick test

Bullous reactions.—A. E. Fischer, B. Rubin, and C. K. Greenwald state that bullous Schick reactions may occur during the acute stage of poliomyelitis, pertussis, pneumonia, measles, scarlet fever, meningococcal meningitis, and erysipelas. No bullous reactions have been noted by the authors in healthy children. These bullous reactions may, or may not, be true positive Schick reactions. The examination of the blood serum of such reactive subjects generally shows the presence of a small amount of antitoxin, sometimes sufficient to indicate immunity. The interpretation of a negative reaction which follows an earlier bullous positive reaction is uncertain. Children tested during the febrile period of an infective disease, in whom bullous Schick reactions develop, should be retested some time after recovery before being considered susceptible to diphtheria.

Treatment

Antitoxin therapy

The 'anti-B' factor in antitoxin.—C. J. McSweeney states that cases of diphtheria at Cork Street Hospital, Dublin, are classified into four grades as follows: Grades 1 and 2 include faucial cases in which the membrane is confined to the tonsils and their pillars, with or without laryngeal involvement, and pure laryngeal cases. In grade 3 the membrane extends

Union

Rôle of oestrogen.—G. A. Pollock and R. K. Ghormley describe the process of bone repair in 21 mature female rats with experimental fracture of the right humerus. One-third of them had previously undergone ovariectomy, another third received 2,000 international units of oestrogen at intervals after fracture, and one-third formed a control group. One rat in each group was killed daily and the bone examined histologically. Seals had gradually been formed across the medullary cavity composed of fibrous plugs of disintegrated red blood cells, fibrin bands, or periosteum strands; in one rat a cortical bone plug was formed which might prevent the union of the bones. Fibroblasts from the bone marrow or from the periosteum invaded the seal which was continuous with the periosteum. After one day, the periosteum was thickened as far as the neck of the humerus, and on the third day sub-periosteal osteoid tissue appeared far removed from the fracture and along the whole bone shaft. Bone tissue from the endosteum contributed to the plug and appeared to be more profuse in the animals treated with oestrogen. Apart from this there were no significant differences between the three groups.

Regional

Wrist joint

Internal fixation of fractured scaphoid.—J. R. Armstrong states that, in dealing with fracture of the carpal scaphoid, immobilization alone does not always produce good results in cases of 'old' fractures or in cases of delayed union. Disturbances of blood supply, even if not sufficient to cause non-vascular necrosis of one fragment, probably account for the delay in union so often seen in these fractures. It is difficult to produce absolute immobilization of the scaphoid for more than a few days with any form of splint or cast compatible with free finger movement. Theoretically the ideal treatment is by internal fixation, but the published results have often been disappointing. The author describes a technique which has given satisfactory results. With the hand palm upward in neutral position, if the wrist be held in 45° pronation, the long axis of the scaphoid lies in the vertical plane at an angle of 50° to the perpendicular. A radiogram with the wrist in this position gives a true lateral view of the scaphoid. Using a rest to hold the wrist in this position, a drill introduced through a small incision on the lateral aspect of the tubercle of the scaphoid and driven inward in the vertical plane at an angle of 50° to the perpendicular, passes through the centre of both fragments of a fractured scaphoid. When the position of the drill has been checked by X-rays, a bone peg from the tibia can be driven along the drill track, impacting and fixing the fracture. This closed technique avoids any exposure or stripping of the bone, and entails no disturbance of its blood supply.

Ankle joint

Osteoarthritis as a complication.—R. W. Lewis and W. C. Graham report on 18 patients with secondary osteoarthritis after fracture of the ankle, and state that age, sex, and probably weight are definite factors in the occurrence of these fractures and in determining their outcome. Protracted symptoms over a period of months following treatment constitute a very unfavourable sign. Fracture of three malleoli and splitting fractures of the lower extremity of the tibia appear to be more prone to lead to secondary osteoarthritis than do fractures of one or two malleoli. Nothing short of mechanically perfect reduction affords a reasonable chance of avoiding secondary osteoarthritis, and even then there is not any positive assurance of escape. Perfect reduction sometimes gives excellent results, even when all other factors are unfavourable.

Foot

Bilateral march fracture.—R. Drummond records a bilateral march fracture in a probationer nurse 23 years of age. It is characteristic of the condition that there is never any history of trauma in the affected foot. At first there is complaint of dull aching pain, which becomes progressive, and demands relief by resting the foot; later, even rest may not afford complete freedom from pain. After a few days or weeks oedema appears on the dorsum of the affected foot, generally over the 2nd or 3rd metatarsal, which may be tender on pressure. Radiography may not show a fracture in the early stages, but there may be a little rarefaction of the shaft or neck of the affected metatarsal. A later radiogram will show a crack fracture with little displacement. At a still later stage there can be seen a large spindle-shaped mass of callus surrounding the line of fracture. Later still there may be only a characteristic spindle-shaped mass of callus due to bony union having been effected. The condition has been confused with osteoma, syphilitic periostitis, and sarcoma. Treatment consists of the application of a walking plaster for a month, followed by strapping and foot exercises. The prognosis is good.

Armstrong, J. R. (1941) *Lancet*, **1**, 537.

Cameron, D. M. (1940) *Proc. Mayo Clin.*, **15**, 561.

Campbell, W. C., and Smith, H. (1941) *J. Bone Jt Surg.*, **22**, 959.

Drummond, R. (1940) *Brit. med. J.*, **2**, 413.

Lewis, R. W., and Graham, W. C. (1940) *Amer. J. Surg.*, **49**, 210.

Pollock, G. A., and Ghormley, R. K. (1941) *J. Bone Jt Surgery*, **23**, 273.

Venable, C. S., and Stuck, W. G. (1941) *Amer. J. Surg.*, **51**, 757.

DISSEMINATED SCLEROSIS

See also B.E.M.P., Vol. IV, p. 187; Cumulative Supplement, Key No. 354; Surveys and Abstracts 1939, p. 316; 1940, p. 277.

Treatment*Artificial fever therapy*

With physical methods.—A. E. Bennett and M. D. Lewis employed artificial fever therapy, with physical methods, in 51 cases of disseminated sclerosis, and followed them up for an average of 31 months. These patients were classified as early, intermediate, and advanced, the disease in the first group being of short duration and the patient able to walk without assistance; in the last group the patients were bedridden and the disease usually of long duration. Of the 10 patients classified as early cases, 8 experienced and maintained worth-while improvement; in 4 of these the findings suggested an infective basis; they all had almost complete remissions. Of the other 6 early cases, 4 made definite prolonged improvement. Of the 25 intermediate cases 13 showed slight to marked improvement. In the 16 advanced cases, only 2 showed any definite arrest of the disease.

Bennett, A. E., and Lewis, M. D. (1940) *J. nerv. ment. Dis.*, **92**, 202.

DIVERTICULOSIS AND DIVERTICULITIS

See also B.E.M.P., Vol. IV, p. 207; Cumulative Supplement, Key No. 355; Surveys and Abstracts 1939, p. 316; 1940, p. 279; and p. 25 of this volume.

Diverticulum of Duodenum*Peri-vaterian duodenal diverticula*

Complications.—R. F. Ogilvie describes 4 peri-vaterian duodenal diverticula found at necropsy and their complications, especially acute necrosis of the pancreas. These occurred in 2 men aged 69 and 34, and 2 women aged 73 and 46. The peri-vaterian duodenal diverticula occur in a particular position, namely in the second part of the duodenum medial to and above the ampulla of Vater, and therefore are different from diverticula in other parts of the duodenum, such as the duodeno-jejunal diverticula recorded by R. W. Raven. Besides his 4 cases, the cases previously reported are discussed. Thus reference is made to two diverticula close together which have been reported. The complications due to the peri-vaterian diverticula are (1) obstruction of the duodenum; this did not occur in any of the author's 4 cases, but 4 examples, one with two diverticula, the larger of which compressed the duodenum and caused dilatation of the stomach, are quoted; (2) obstruction of the common bile-duct; this was present in 10 other recorded cases, and in 3 of the author's 4 cases; (3) dilatation of the pancreatic (Wirsung's) duct as well as of the common bile-duct (1 case); (4) acute necrosis of the pancreas; this supervened in 3 of the author's 4 cases, and in 5 of those previously published; in 4 of these 5 cases, in which the state of Wirsung's duct is mentioned; it was normal in 1 and dilated in 3. The author concludes that obstruction of the pancreatic duct was the cause of acute necrosis of the pancreas. Inflammation of the peri-vaterian diverticulum, duodenitis, peri-diverticulitis, perforation, and primary carcinoma are very seldom reported. There was an enterolith in one of the author's cases.

Treatment*Diverticulitis*

Obstruction and colostomy.—E. S. Judd reports the case of a woman, aged 67, with obstructing diverticulitis of the sigmoid colon, in which the obstructing mass was removed by resection. The distal loop was so short that a single-barrelled colostomy was performed by using the proximal loop, and the distal loop was closed. Some months later the colonic stoma appeared normal, and was functioning satisfactorily. The patient, however, insisted that the stoma be closed. Proctoscopic examination showed that the distal segment of the colon was normal. The closed end of the distal segment was opened. The proximal loop was dissected from the abdominal wall at the site of the stoma, and the continuity of the intestine was restored. Normal action of the bowels was successfully restored.

Judd, E. S. (1941) *Proc. Mayo Clin.*, **16**, 117.

Ogilvie, R. F. (1941) *Brit. J. Surg.*, **28**, 362.

Raven, R. W. (1939) *Lancet*, **1**, 203.

DROWNING: RESUSCITATION

See also B.E.M.P., Vol. IV, p. 233; Cumulative Supplement, Key Nos. 357 and 358.

Resuscitation*Artificial respiration*

Indications for prone pressure method.—Y. Henderson and J. M. Turner state that, when natural breathing is stopped, it is restored more effectively by manual artificial respiration than by mechanical respiration. The latter, unless it is so forcible as to be harmful, does not increase the volume of natural breathing. The best method of resuscitation from drowning and electric shock is prone pressure artificial respiration supplemented by inhalation of carbon dioxide and oxygen. The best method of resuscitation from carbon monoxide asphyxia is inhalation of carbon dioxide and oxygen, initiated in severe cases by prone pressure artificial respiration.

Henderson, Y., and Turner, J. M. (1941) *J. Amer. med. Ass.*, **116**, 1508.

DRUG ERUPTIONS

See also B.E.M.P., Vol. IV, p. 261; Cumulative Supplement, Key No. 360; and Surveys and Abstracts 1939, pp. 176 and 319; 1940, p. 280.

Common Drug Eruptions*Purpura haemorrhagica due to arsphenamines*

E. H. Falconer, N. N. Epstein, and Edith S. Mills report 7 cases seen since 1933 of hypersensitivity to the arsphenamines (6 to neo-arsphenamine and 1 to bismarsen). The patients gave reactions accompanied by idiopathic thrombopenic purpura. Other workers have described a relation between deficiency of vitamin C and sensitivity to arsphenamine and the clinical use of vitamin C to obviate the toxic effects of arsphenamines and the therapeutic effect of ascorbic acid in patients with idiopathic thrombopenic purpura. These reports have been conflicting. Falconer, Epstein, and Mills gave their 7 patients vitamin C in crystalline form as ascorbic acid, orally or parentally in varying amounts, to determine whether or not this modified the subsequent reactions to the injection of arsphenamines. They found that at no time and in no patient was there any appreciable modification of sensitivity reaction during or after administration of vitamin C. The apparent increase in severity of the reaction after the administration of vitamin C in 3 of these patients was probably due entirely to increased sensitivity as the result of previously administered arsphenamine.

Bromide eruptions

Treatment by adrenal cortex and sodium chloride.—C. P. Bondurant and C. Campbell find that the administration of adrenal cortex and sodium chloride appears to be of value in assisting the excretion of bromides and in bromide intoxication. Treatment consisted of 10 grammes of sodium chloride by mouth daily and 5 cubic centimetres of adrenal cortex by intramuscular injection. Mental symptoms and skin eruptions appeared to clear up more quickly than by other methods of treatment.

Sulphapyridine eruptions

Generalized skin lesions.—L. W. La Towksy reports 3 cases of severe skin reactions during the use of sulphapyridine (M & B 693) for gonococcal urethritis. In each case the eruption was generalized. At various times the lesions were maculo-papular, vesicular, pustular, and bullous. All the patients had had severe itching and showed desquamation of the skin. Associated generalized discrete enlargement of the lymphatic glands also occurred.

Bondurant, C. P., and Campbell, C. (1941) *J. Amer. med. Ass.*, **116**, 100.

Falconer, E. H., Epstein, N. N., and Mills, Edith S. (1940) *Arch. intern. Med.*, **66**, 319.

La Towksy, L. W., Uhle, C. A. W., and Knight, F. (1941) *Med. Times, N.Y.*, **69**, 120.

DUPUYTREN'S CONTRACTION

See also B.E.M.P., Vol. IV, p. 272.

Clinical Picture*Advanced condition*

Microscopic investigation.—H. W. Meyerding, J. R. Black, and A. C. Broders show that Dupuytren's contraction is not merely a disease of the palmar fascia, but involves all structures from the skin down to the tendon sheaths. It is difficult therefore to understand how subcutaneous tenotomy could give consistently good results. The authors studied microscopic sections of the palmar fascia in 57 cases of the disease and form the opinion that the pathological picture is best explained on the basis of a chronic inflammatory process.

Meyerding, H. W., Black, J. R., and Broders, A. C. (1941) *Surg. Gynec. Obstet.*, **72**, 582.

DYSENTERY, BACILLARY

See also B.E.M.P., Vol. IV, p. 317; Cumulative Supplement, Key No. 364; Surveys and Abstracts 1939, p. 320; and p. 6 of this volume.

Treatment*Sulphanilylguanidine*

E. K. Marshall, Jun., A. C. Bratton, Lydia B. Edwards, and Ethel Walker employed sulphanilylguanidine in the treatment of acute bacillary dysentery in both children and adults. The children included 17 cases in which the diagnosis was confirmed by recovery of the dysentery organism from the stools. An advantage of the drug is that saturation of the intestinal contents can be obtained with a dosage which gives a low concentration in the blood. Treatment was generally begun within 24 hours of admission to hospital or as soon as the probable diagnosis of dysentery was made. Initial doses of the drug were either 0.1 or 0.2 gramme per kilogram of body weight; maintenance doses varied from 0.1 gramme per kilogram every 8 or 12 hours to 0.05 gramme per kilogram every 4 hours. Other aspects of management of the patients were those standard for such disorders. Frequent stool cultures were made during the first few days of treatment. In 7 children in whom treatment was begun on or before the third day of the disease, the results were uniformly good. All were young children under 5 years of age; all had high fever before treatment was begun; 4 had had convulsions; and 6 of the 7 were seriously ill. Within 28 hours, and often sooner, after the drug was begun, the temperature had fallen to below 100.4° F. in every case, and the children remained afebrile during the rest of their stay in hospital. Within 12 to 36 hours there was

a striking improvement in the general condition, some of the children appearing almost well after only 24 hours of chemotherapy. The diarrhoea was checked in from 1 to 3 days in all children given the drug on a 4-hourly schedule; 2 children given the drug 12-hourly did not establish normal stools until the sixth and seventh day respectively, although the temperature fell and the general condition improved markedly within 24 hours after treatment was begun. In 10 children treated late in the disease, from the fourth to the fourteenth day, the results were not so uniform. Some showed the same striking improvement as in the early group, but most ran a course uninfluenced by the drug. In 10 of the total of 17 children the stool cultures became negative for dysentery organisms between treatment, and remained negative during their stay in hospital. In 5 other cases the stools became negative on the last day of therapy, or within 2 days of its discontinuance.

Marshall, E. K., Jun., Bratton, A. C., Edwards, Lydia B., and Walker, Ethel
(1941) *Johns Hopk. Hosp. Bull.*, 68, 94.

DYSMENORRHOEA

See also B.E.M.P., Vol. IV, p. 353; and Surveys and Abstracts 1939, p. 321; 1940, p. 282.

Aetiology

Uterine contractions

There are many hypotheses to explain functional dysmenorrhoea, but none of them adequately explain all cases. L. Wilson and R. Kurzrok regard the condition as due to a reduction of the pain threshold, due either to psychological causes or possibly to a factor related to the pathways in the presacral sympathetic nervous system. They examined 29 patients by the intra-uterine balloon method which measures uterine contractions. Altogether 239 records were made during 98 menstrual cycles. A control group of 29 women with normal menstruation or disturbances other than dysmenorrhoea were also examined, and 351 tracings were made on them. During the middle two weeks of a normal menstrual cycle the uterine contractions are of small amplitude and short duration, and the interval between contractions is short and tonus is high. In the week preceding menstruation contractions increase in amplitude and duration, and decrease in frequency and tonus. During the next week there is a gradual return to the intermenstrual condition of small amplitude. It thus appears that the pain coincides with the period of maximal uterine contractibility. In anovulatory cycles, in which the luteal phase is absent, these large contractions do not occur and there is no pain. In all the 29 patients with dysmenorrhoea no alteration from the normal myometrial cycle was observed; thus no support was found for the hypothesis that excessive uterine contractions are the cause of the pain; in fact in one woman in whom the pressure within the balloon exceeded the systolic blood pressure after injection of pituitrin, there was no pain. The authors have tried hormonal therapy of various kinds and will report on their results elsewhere. They consider that the beneficial effect of gonadal hormone early in the menstrual cycle may be attributed to reduction of uterine motility only if the next menstruation occurs prematurely.

Treatment

Benzedrine sulphate

Z. E. Taylor reports good results from the use of benzedrine sulphate in 34 cases of essential dysmenorrhoea. It was tried because it relaxes smooth muscle in general, and at the same time increases the sense of well-being. The patients were given 3 trial doses of 2.5, 5.0, and 10 milligrams of benzedrine sulphate during intermenstrual periods, and were observed for an hour to determine whether or not any sensitivity to the drug or untoward reactions occurred. The patients were then instructed to take 10 milligrams of the drug before breakfast for 2 days before the next expected period and on the first day of the period, and to repeat the dose if the pain was not relieved. They were not allowed to take more than 20 milligrams daily, or to take a second dose after 2 P.M. without the advice of the medical practitioner. Treatment lasted for 3 or 4 days, depending on the expected duration of symptoms. The drug relieved pain, fatigue, and depression in women in whom other measures had failed. This was confirmed by the substitution of placebos or other medication during alternate periods. In more than 40 per cent of patients complete relief was obtained, and in an equal percentage moderate relief occurred. The author concludes that benzedrine sulphate is a valuable drug for the treatment of dysmenorrhoea, and that it is suitable for use in ambulatory patients. Any objections to the use of benzedrine sulphate in such cases on account of reactions can be met by making preliminary tests.

Taylor, Z. E. (1941) *New Engl. J. Med.*, 224, 197.

Wilson, L., and Kurzrok, R. (1940) *Endocrinology*, 27, 23.

DYSPEPSIA

See also B.E.M.P., Vol. IV, p. 367; and Surveys and Abstracts 1939, p. 321.

Clinical Picture

Incidence in the armed forces

Causal Factors.—H. L. Tidy, in opening a discussion on dyspepsia in the Forces at the Medical Section of the Royal Society of Medicine, divided the subject into (1) peptic ulcer, (2) functional dyspepsia, and (3) transient dyspepsia. He drew attention to the great increase

in dyspeptic conditions in the population generally during the last 20 years, and discussed the question whether or not the incidence in the Army was higher than in civilian life. Relapses seemed to occur more quickly under Army conditions, owing partly to food and cooking; the food in the Army was more liberal and heavier than that in civil life. In the early months of this war cooking had been deficient in some respects, but had now been very greatly improved. The significance and importance of a relapse in the Army were much greater, for the patient had to go to hospital, whereas a civilian could lie up and diet at home for a day or two. Psychological factors did not exert much influence in the soldier. There were many cases of gastritis, and on the whole these were less responsive than peptic ulcer to treatment, and more prone to psychological factors.

C. E. Newman referred to the differential diagnosis between duodenal ulcer and duodenitis, and between an organic lesion and a neurotic disorder; in many of the organic cases there was also a neurotic element. The diagnosis of gastritis was predominant in patients sent home in 1940 from the British Expeditionary Force, but it was rare. With this J. G. Scadding agreed, but it was rare in civilian practice; the recent tendency to describe soldiers with dyspepsia as the subjects of 'soldier's stomach' rather than the analogy of 'soldier's heart' was unfortunate. Scadding reported on his examination of 137 cases of dyspepsia in soldiers. Among 57 cases of proved ulcer 6 only originated in the Army, the others having shown symptoms previously in civilian life. It was very difficult to assess the psychological element: in only 9 of the 137 patients was an obvious psychological abnormality detected.

A. F. Hurst raised the question to what extent might radiological reports be misleading, especially as regards the diagnosis of a duodenal ulcer on the evidence of the scar of a healed ulcer. According to R. T. Payne, malingering was too often suspected by medical officers, and many mistakes were due to leaving the final diagnosis to the radiologist or someone without all the available data.

J. G. Graham and J. D. O. Kerr, from experience during 14 months in a home military hospital for all branches of the fighting services, including the Women's Auxiliary Services, find that the only disease showing an overwhelming increase during the war has been in the group of disorders of the gastro-intestinal tract. Thus among 790 medical admissions to a North-Western hospital there were 246, or 31 per cent, made up of 135, or 55 per cent, of duodenal ulcer, 14 being officers, but no women; of gastric ulcer there were only 23, of gastritis 60, or nearly 25 per cent, and a miscellaneous group of 28 cases including cholecystitis, abdominal adhesions, mucous colic, and catarrhal jaundice; in this group there were 4 females. The experience of much the same character is quoted from a military hospital in a North-Eastern area, where among 980 medical admissions 353, or 36 per cent, were for gastro-intestinal disorders. These figures correspond with those pointing to the same prominence of gastro-intestinal disorders in war conditions, especially of duodenal ulcer. The vast majority of peptic ulcer cases were exacerbations of an old-standing condition which had been adequately dealt with in civil life by simple medical treatment, enabling the patient to do his work, but which broke down in the face of the strain of war. Complications, such as haematemesis and perforation, were rare.

Differential Diagnosis

Radiological diagnosis

In soldiers.—R. Saffley analyses the radiological results of examination of 320 soldiers with dyspepsia and an average age of 32 years. Of these 161 were normal, and the majority of these are sent to the Army psychiatrists who may or may not refer them for invaliding. The main object of the radiological examination is the detection of peptic ulcer; if found the patient is almost always invalided out of the Army. Duodenal ulcer was diagnosed in 111, or 35 per cent, and gastric ulcer in 13, or 4 per cent, in none of which there was any evidence of malignant disease. These results are compared with those recently obtained by others (H. Morris; R. T. Payne and C. E. Newman; and P. H. Willcox).

Cutaneous abdominal hyperaesthesia in dyspeptics

In soldiers.—W. G. Mills, anxious to find an easily applied test to differentiate organic disease, such as peptic ulcer, from other causes of dyspepsia in soldiers, reports the results of examination of 30 soldiers with dyspepsia by (1) mapping out cutaneous hyperaesthesia and (2) by radiological means. It was found that in no case with cutaneous hyperaesthesia was the radiogram normal, and that the presence of hyperaesthesia 'coincided considerably with abnormal radiological findings'. In 7 only of the 30 cases was cutaneous hyperaesthesia absent; in 21 it was above the umbilicus, 9 being bilateral, 11 on the right side, and 1 on the left side. This publication called forth from Hurst a vigorous protest against an attempt to revive a method of diagnosis 'which had been allowed to fall into well-merited oblivion for twenty years'. After reading in 1903 Head's work on the association of cutaneous hyperaesthesia with visceral disease, he mapped out Head's areas in a large number of cases. In 1909 he examined 9 patients with duodenal ulcer the day before they were operated upon by Moynihan, and greatly to his surprise failed to discover cutaneous hyperaesthesia in any of these phlegmatic middle-aged Yorkshiremen. He soon realized that the patients previously examined were mainly highly suggestible chlorotic girls who were not suffering from gastric ulcer, and since then, by taking care to avoid suggestion, has never found cutaneous hyperaesthesia in any of hundreds of cases of ulcer. On the other hand, he has often removed an area of hyperaesthesia by suggestion, replaced it by anaesthesia, or transferred it to the opposite

side after it had been marked out by a clinical clerk. Emphasis is laid on the remarkable suggestibility of the average soldier.

Graham, J. G., and Kerr, J. D. O. (1941) *Brit. med. J.*, **1**, 473.

Hurst, A. F. (1941) *Brit. med. J.*, **1**, 415.

— (1941) *Proc. R. Soc. Med.*, **34**, 422.

Mills, W. G. (1941) *Brit. med. J.*, **1**, 315.

Morris, H. (1940) *Brit. med. J.*, **2**, 235.

Newman, C. E. (1941) *Proc. R. Soc. Med.*, **34**, 417.

Payne, R. T. (1941) *Proc. R. Soc. Med.*, **34**, 424.

— and Newman, C. (1940) *Brit. med. J.*, **2**, 819.

Saffley, R. (1941) *Brit. J. Radiol.*, **14**, 96.

Scadding, J. G. (1941) *Proc. R. Soc. Med.*, **34**, 418.

Tidy, H. L. (1941) *Proc. R. Soc. Med.*, **34**, 411.

Willcox, P. H. (1940) *Brit. med. J.*, **1**, 1008.

EAR DISEASES

See also B.E.M.P., Vol. IV, p. 402; Cumulative Supplement, Key Nos. 374-384; Surveys and Abstracts 1939, pp. 86, 94, and 322; 1940, pp. 46 and 283; and p. 52 of this volume.

Acute Otitis Media

Complications

Convulsions.—N. Asherson, discussing the treatment of convulsions of otogenic origin, states that, at the onset of acute earache, the ears should be examined, and a myringotomy performed, the pus being sent for culture to ascertain the organism. If there is any suspicion of nuchal rigidity, an immediate lumbar puncture is indicated. If the acute otitis media is well established, a lumbar puncture is at once performed with precise manometric measurements of the fluid pressure, and the fluid immediately submitted to a complete cytological, chemical, and bacteriological examination. A complete neurological examination is made, followed by a mastoid operation with exposure of the dura of the temporal lobe. The dura and temporal lobe should be explored by brain puncture, after the extended mastoid operation has excluded the presence of an extra-dural abscess in the middle cranial fossa. The lateral sinus should also be explored by puncture. The radical mastoid operation is not, as a rule, necessary. In the presence of a chronic ear discharge immediate radical mastoid operation with extensive exposure is performed.

Treatment

Sulphanilamide.—J. W. Babcock reports on the use of sulphanilamide in 45 cases of acute otitis media and compares the results obtained in 48 cases in which the patients did not receive the drug. All the patients were children of from 6 months to 10 years of age. All received prompt myringotomy, none being treated by the drug alone. In both groups accompanying disease of the nose or throat was treated, and the ears were treated by dry wipes or irrigations. It was found that, on the whole, the results in the two groups differed little. The percentage, however, of the treated group requiring operation was higher than that of the control group. The author considers that the effect of sulphanilamide on acute otitis media is somewhat overrated.

J. B. Jessiman employed sulphanilamide successfully in 7 cases of acute suppurative otitis media with bulging of the drum, in children. Treatment was begun early, and the dosage of the drug was $7\frac{1}{2}$ grains, crushed or chewed, every 4 hours for the first 2 days, and reduced on alternate days until the patient was receiving 2 tablets only on each of the 2 last days of treatment. The average total dosage was 225 grains given over an average of 7 days. Paracentesis was not performed, nor any other local treatment given.

W. C. Bowers analyses 793 cases of acute purulent otitis media in 396 of which sulphanilamide was employed. He concludes that, if sulphanilamide is given early, before bone destruction occurs, the duration of discharge is diminished by about 50 per cent; after uncomplicated mastoidectomy, the drug should not be given; complicated mastoiditis requires intensive chemotherapy; and sometimes it is necessary to stop the drug in order to obtain a true picture, since the drug cures disease of the middle ear while progressive bone destruction is active in the mastoid. The dosage suggested is 0.06 gramme per pound of body weight up to 90 lb., every 24 hours. During the first 24 hours this amount is doubled, tripled, or quadrupled, according to the severity of the infection and the type of patient. Chemotherapy is a valuable aid in otolaryngology, but should be used cautiously in view of its tendency to obscure the clinical picture.

Complications of Suppuration in the Middle Ear

Extra-dural abscess

Disclosure of congenital absence of lateral sinus.—H. L. Williams and O. E. Hallberg report a case of congenital absence of the cranial venous sinuses on the right side. The child was admitted to hospital with acute osteomyelitis of the lower portion of the humerus. A blood culture showed the *Streptococcus haemolyticus*. There was discharge from the right ear, and some tenderness over the right mastoid process. At operation the right mastoid antrum was found to be filled with pus. In an attempt to uncover the sigmoid sinus, a huge epidural

abscess was found. After evacuation of the pus and removal of infected granulation tissue from the dura, evidence of the sigmoid or lateral sinus could not be found.

Meningitis

W. Williams reviews 40 cases of otogenous meningitis from which 4 of the patients recovered. There were 28 males and 12 females; 9 of the patients were under 10 years of age, 12 under 20, 3 under 30, 4 under 40, 7 under 50, 4 under 60, and 1 was 62. In 28 of the cases meningitis was preceded by acute otitis. In 10 cases the otitis was chronic, and in 2 cases the otitis was of a few months' duration and might be called subacute. In 36 cases the focus of infection was extra-labyrinthine, and in 4 labyrinthine. In the former group there were at least 5 cases of petrositis, 6 of cerebral abscess, 2 of cerebellar abscess, and 3 of sinus thrombosis. Streptococci were present in 14 cases, pneumococci in 5 cases, and in 2 cases Gram-positive organisms were found. In 31 cases a Schwartze mastoid operation was the first procedure, and in the others a radical mastoidectomy was performed.

Asherson, N. (1940) *J. Laryng.*, **55**, 303.

Babcock, J. W. (1940) *Arch. Otolaryng.*, Chicago, **32**, 246.

Bowers, W. C. (1940) *J. Amer. med. Ass.*, **115**, 178.

Jessiman, J. B. (1941) *Brit. med. J.*, **1**, 399.

Williams, H. L., and Hallberg, O. E. (1941) *Arch. Otolaryng.*, Chicago, **33**, 78.

Williams, W. (1941) *Aust. N.Z. J. Surg.*, **10**, 249.

ECTHYMA

See also B.E.M.P., Vol. IV, p. 442.

In Adults

Ecthyma contagiosum

Virus disease of sheep.—R. Nomland reports 2 cases of local inoculation in man of ecthyma contagiosum, a virus disease of sheep. Lesions appeared on the fingers and thumbs in the form of red painful swellings which proceeded to blister formation. These ruptured and progressed to form crusts surrounded by pus-filled tense bullae, surrounded in turn by an inflammatory areola. The lesions healed without complications in a few weeks.

Nomland, R. (1940) *Arch. Derm. Syph.*, N.Y., **42**, 878.

ELECTRICAL INJURY

See also B.E.M.P., Vol. IV, p. 472.

Clinical Effects

Deeper structures of arm

Unusual type of injury.—F. H. Hesser describes an unusual type of injury sustained by contact with a 2,400-volt circuit. The patient, a man aged 29, received a severe shock in the left arm which became weak and later became swollen, hot, painful, and partially paralysed. Spontaneous and recurrent bruises appeared, but there was no injury to the external skin. Operation showed deep areas of haemorrhage, liquefaction of fat, thrombosis of small vessels, a 'cooked' appearance and disintegration of muscle tissue. The walls of the blood vessels were brittle and friable. The joints were not damaged. The accumulation of dead tissue and blood clot set up systemic reactions in the form of vomiting and nausea. Damage to nerve function was masked by severe damage to the muscles. Drainage of the sero-sanguineous discharge relieved the pain. It is suggested that contact with the current was imperfect and that the skin acting as an insulator confined it to the deeper tissues. It diffused into the trunk and did not cause further damage. Interference with the circulation was probably responsible for the muscular paralysis and for the slowness in tissue repair, which consisted chiefly of scar tissue. The injury is thought to be due to the heat generated by the current. There is little hope for a return of function.

Hesser, F. H. (1941) *Johns Hopk. Hosp. Bull.*, **68**, 388.

ELECTROTHERAPY

See also B.E.M.P., Vol. IV, p. 490; Cumulative Supplement, Key No. 389; and Surveys and Abstracts 1939, p. 326; and p. 80 of this volume.

Direct Current

Ionization

Pelvic iontophoresis.—C. A. Gordon and A. H. Rosenthal employed pelvic iontophoresis of a choline compound in 58 cases of subacute and chronic pelvic infection, all of which were severe enough to warrant removal of the patients to hospital. Of these cases 37 were of tubo-ovarian infection and 21 were cases of cellulitis. In most cases subjective improvement was marked, and often was out of proportion to objective evidence of decrease of the infection. The results of treatment in tubo-ovarian infections, although often good, are not sufficiently remarkable to warrant routine use of this treatment. The best response was in cases of massive cellulitic infection of recent origin which had failed to yield to ordinary treatment.

High-Frequency Currents

Effect on the body

Importance of magnetism.—K. F. Nagelschmidt, discussing the specific effects of high-frequency currents and magnetotherapy, suggests that the production of small currents in

the body through the influence of external magnetic fields must have some definite effect on the general and local muscle tone, on the conductivity of the nerves in both directions, on the shape of the electrocardiogram, on the brain currents, and probably on the balance of the vegetative nervous system. The author believes that magnetic forces are not unimportant to life, and that their investigation opens up a new and wide field of biological and medical research.

Low-Voltage Varying Currents

Faradic currents

Used for shock-therapy in mental disease.—A. Myerson describes the application of electric shock treatment to 36 patients with mental disorders. A specially made electrical apparatus was used; the practical and reasonable safety of the method has been widely confirmed. It is pleasanter than the leptazol convulsion method and equally effective. All but 2 of 24 patients with depression showed some improvement. There were 9 cases of schizophrenia and 3 of chronic neurosis in which no considerable or sustained improvement was obtained. The average number of shocks given was between 5 and 6. For the majority of patients a voltage of 70 with a milliamperage of 350–500 delivered for 0.1 second was sufficient to produce instantaneous or almost instantaneous shocks lasting from 30 to 45 seconds. No harmful effects were observed, but there was often a temporary disturbance of memory. Although patients with heart disease or hypertension should not be treated by this method (unless their mental condition is likely otherwise to prove fatal), 2 patients with these disabilities were successfully treated. Shocks should be few in number and should be followed by long intervals for the observation of results. The treatment may be given at the out-patient department, and may take place even in a private house with adequate attendance.

Gordon, C. A., and Rosenthal, A. H. (1941) *Amer. J. Obstet. Gynec.*, **41**, 237.

Myerson, A. (1941) *New Engl. J. Med.*, **224**, 1081.

Nagelschmidt, K. F. (1940) *Brit. J. phys. Med. N.S.*, **3**, 201.

EMBOLISM, ARTERIAL

See also Surveys and Abstracts 1940, p. 286.

Aetiology

Mural thrombi

Pathological data.—In order to determine the importance of mural thrombi in the cardiac cavities as a source of emboli, C. F. Garvin analyses the clinical and pathological data from necropsies of 771 cases of cardiac disease among 6,285 consecutive necropsies from January 1930 to June 1939 at the Cleveland City Hospital, Ohio. If mural thrombi play an important part as a source of emboli, then the necropsies showing the presence of mural thrombi should present a significantly higher incidence of infarction of the various viscera than do cardiac cases without mural thrombi. On the right side of the heart there were one or more mural thrombi in 161 cases, and of these 93, or 58 per cent, showed one or more pulmonary infarcts; whereas of the remaining 610 cases, which did not show mural thrombi, there were 128 instances of pulmonary infarction, an incidence of 21 per cent. On the left side of the heart there were mural thrombi in 193 cases and of these 94, or 48.7 per cent, showed one or more infarcts in the brain, kidneys, spleen, intestines, and/or the extremities. In the 578 cases without mural thrombi there were 135 instances of infarction in the body, an incidence of 23.4 per cent. In hypertensive heart disease and in coronary artery disease with or without myocardial infarction the incidence of pulmonary infarction in the presence of mural thrombi in the right side of the heart was three to four times as high as in their absence. In rheumatic heart disease the incidence of pulmonary infarction was more than twice as high with thrombi in the right side of the heart. Infarcts in the brain, kidneys, spleen, intestines, or the extremities occurred two to four times more often in hypertensive heart disease when mural thrombi were present in the left side of the heart than when they were absent. In coronary artery disease with myocardial infarction and in rheumatic heart disease, infarcts involving the brain, kidneys, spleen, intestines, and/or extremities were about twice as frequent when mural thrombi were present in the left side of the heart. In coronary artery disease without myocardial infarction, infarcts in the brain, kidneys, spleen, intestines, and/or the extremities were 1.7 times as frequent when mural thrombi were present in the left side of the heart as in their absence: but this difference, unlike the others, was not regarded as statistically significant. These observations show that mural thrombi in the heart are a significant cause of embolic occlusion of arteries in both the lesser and greater circulations.

Treatment

Embolectomy

Prevention of gangrene.—R. R. Linton emphasizes with quoted statistics the great importance of immediate embolectomy in order to prevent gangrene of the extremity. Thus, the loss of a limb may be due to the failure of the medical practitioner who first sees the patient either to make a correct diagnosis or to realize the fundamental need for early treatment. Very little has been written about the pathological changes that take place in the arteries of an extremity after the lodgement of an embolus and the significance of changes in reference to restoration of function. Failure to restore the circulation in an extremity after embolism is primarily due to the severe vasoconstriction distal to the embolism, and the formation of a

secondary thrombus in the arterial tree, which extends distally from the site of the embolus into all the branches. It is due to the extreme degree of vasoconstriction and the slowing of the blood stream. It has not been settled whether the thrombosis begins at the extreme distal site and spreads upwards to the embolus or in the reverse direction. The vasoconstriction probably begins directly after the embolism, and the treatment consists in removal of the embolus and to induce dilatation of the vessels, by interruption of the vasoconstrictor impulses from the sympathetic by a novocain or alcohol injection of the lumbar ganglia. The formation of a thrombus proximal to the embolus does not spread so extensively as that distal to the embolus, and can be easily removed.

Garvin, C. F. (1941) *Amer. J. med. Sci.*, **201**, 412.

Linton, R. R. (1941) *New Engl. J. Med.*, **224**, 189.

EMPHYSEMA OF THE LUNGS

See also B.E.M.P., Vol. IV, p. 508; Surveys and Abstracts 1939, p. 327; and p. 71 of this volume.

Chronic Obstructive Emphysema

Aetiology

Tuberculous obstructive emphysema in children.—Beryl Barsby reports 3 cases of tuberculous obstructive emphysema in children, and reviews 16 cases previously recorded. The highest incidence of the condition is between the ages of 6 and 12 months; the condition is rare after the age of 6 years. The early age of incidence may be explained by the small lumen of the bronchi, which is easily occluded by enlarged hilar glands secondary to primary infection of the lung, and that the soft bronchial wall yields first to pressure and then becomes ulcerated. Obstructive emphysema may be the first presenting clinical feature in tuberculous children.

Functional impairment

Significance in young patients.—P. M. Andrus insists on the importance of an emphysematous form of chest without any history of causal disease in children or adults under the age of 40. Especially in connexion with recruiting this 'abnormal depth of thorax' calls for further examination by radiology, as it may be evidence of disease of the lungs not yet otherwise accompanied by clinical evidence. An abnormal 'depth of the thorax', even when slight, is a signal that important injury has fallen on the lungs although corroborative evidence is slight or absent. Such individuals are abnormally susceptible to recurrent and protracted respiratory attacks, often pneumonia, and should therefore be regarded as unfit for military service.

Andrus, P. M. (1941) *Canad. med. Ass. J.*, **44**, 344.

Barsby, Beryl (1941) *Lancet*, **1**, 627.

EMPHYEMA

See also B.E.M.P., Vol. IV, p. 520; Cumulative Supplement, Key Nos. 396–398; Surveys and Abstracts 1940, p. 286; and p. 71 of this volume.

Acute Empyema

Treatment

Operation.—F. J. Colahan comments on the high mortality rate among empyema patients who have been discharged but not properly cured and advocates certain principles in the treatment of the disease. The site for drainage should be near the centre of the infected area, as this region heals first. Strong emphasis is laid on pre-operative and post-operative X-ray examinations. Open drainage must be avoided in synpneumonic empyema. Aspiration is harmless except in the presence of lung abscesses, but it should be limited to 1,000 cubic centimetres in the presence of much fluid. Repeated aspiration is not recommended; as complete evacuation is seldom achieved, there is no incentive to lung expansion, and fibrosis may set in before drainage is over, leading to chronic infection. In closed drainage 2–3 cubic centimetres of a 2 per cent solution of novocain should be injected down the pleura and the largest possible self-retaining catheter inserted and connected to a negative pressure drainage apparatus. Negative pressure should be rapidly raised to 12–15 cubic centimetres of mercury, but momentary decompression may be necessary when excessive suction is painful. After 3 or 4 days lavage may be carried out. Alternate negative pressure and antiseptic fluid injections may be applied until the return is clear, followed by strong suction (Morelli's technique). Expanded lungs are thought to react well to infection. Thoracotomy may be necessary if drainage is unsatisfactory. In metapneumonic empyema open drainage is advisable. When the thick fibrous deposit is peeled from the visceral pleura, the lung will often expand. The cavity should be carefully cleaned. Drainage tubes should never be removed before the cavity is obliterated. Intrapleural use of sulphamylamide is thought to be dangerous, but taken orally the drug is valuable. A diet of high calorific value and vitamin content is recommended.

Colahan, F. J. (1941) *Aust. N.Z. J. Surg.*, **10**, 374.

ENCEPHALITIS EPIDEMICA

See also B.E.M.P., Vol. IV, p. 546; Cumulative Supplement, Key No. 399; and Surveys and Abstracts 1939, p. 327; 1940, p. 287.

Definition

Differentiation of viruses

R. S. Muckenfuss reviews the problem of the disease described as lethargic encephalitis by von Economo in 1917. When the adjective 'lethargic' was recognized as a misnomer, it was changed to 'epidemic'. For a time this term seemed satisfactory, but in 1924, 1927, and in several subsequent years a different form of encephalitis occurred in Japan and was called type B to distinguish it from type A, as Economo's form was then designated. Then in the late summer of 1933 and 1937 came the epidemics at St. Louis, Mo., which, though in many respects resembling the Japanese disease, was shown to be of a different aetiology. Recently encephalitis in the spring and early summer in Russia and Siberia, caused by a virus immunologically different from the viruses of the Japanese and the St. Louis forms, has been described. It is thus evident that the term 'epidemic encephalitis' must be broadened and that its use alone is not any longer sufficient as a diagnosis without further definition indicating the forms mentioned above, and also the Australian X disease, of which much more information is desirable. Epidemic encephalitis must now be considered as a general title for a number of virus infections of the central nervous system. The differentiation of these forms must be made in the laboratory where aetiological work or neutralization tests can be carried out to establish the diagnosis. The method of spread of these diseases is for the most part unknown, but some appear to have a reservoir in lower animals and to attack man through the bites of insects.

Treatment

Parkinsonism

Syntropan.—N. S. Schlezinger and B. J. Alpers report on the use of syntropan (3-diethyl-amino-2 : 2-dimethylpropyl tropate) in 16 cases of Parkinsonism, all but one after encephalitis epidemica, for periods varying from 10 days to 8 months. Syntropan has been chiefly used as an anti-spasmodic of smooth muscle, but is 20 times less powerful than atropine; it is free from the unpleasant toxic effects of atropine, but is 100 to 1,000 times less effective on the pupil, saliva, and vagus than atropine. The dosage varied from 1,200 to 2,400 milligrams daily, but it was clear that a dosage less than 1,200 milligrams daily had not any effect, and there is thus reason to question the good effects that have been reported from smaller dosage. Of 14 patients who were potentially capable of tolerating this dose, 10, or 71 per cent, showed mild or moderate symptomatic relief, without the occurrence of any toxic manifestations. Five of the patients did not show any improvement, 2 did not collaborate properly, 2 were intolerant to the drug, and 1 was in an advanced stage of paralysis agitans. Five of the patients were given syntropan in doses as large as 3,200 milligrams daily, and 3 of these showed more alarming toxic symptoms than any noted previously. They were chiefly referable to the nervous system, namely, confusion, sluggishness, drowsiness, and trance-like episodes in which there was a sense of impending death. Syntropan appeared to be useful in many cases in which atropine could not be used because of the frequently associated toxic symptoms.

Muckenuss, R. S. (1941) *Bull. N.Y. Acad. Med.*, 2 ser., **17**, 487.

Schlezinger, N. S., and Alpers, B. J. (1941) *Amer. J. med. Sci.*, **201**, 374.

ENCEPHALO-MYELITIS

See also B.E.M.P., Vol. IV, p. 553; Cumulative Supplement, Key No. 400; and Surveys and Abstracts 1939, p. 328.

Acute Disseminated Encephalo-Myelitis Complicating the Specific Fevers and Vaccination

Terminology

New conceptions and allied forms.—In a critical article entitled 'Newer Conceptions of Post-infectious and related Forms of Encephalitis', T. J. Putnam, professor of neurology and neurosurgery, College of Physicians and Surgeons, Columbia University, writes: 'As a result of a prevalent convention of recent origin, and with no sound basis in derivation, the term is confined by many pathologists to conditions characterized by inflammatory phenomena'. With regard to epidemic encephalitis he remarks: 'A peculiar position is occupied by lethargic encephalitis; there was an epidemic 20 years ago. It was generally considered to be an infective disease, but no proof of its infectious nature has ever been brought out. Cases of lethargic encephalitis are now extremely rare, if indeed any authentic ones occur, and the acute disease is no longer a practical problem.' Putnam urges the recognition of conditions, among those called 'encephalitis' or 'encephalo-myelitis', due not to inflammation or infection, but to thrombosis of the small blood vessels of the white matter, the primary change being in the clotting mechanism of the blood.

Due to toxoplasma

Atypical cases.—A. B. Sabin reports 2 cases of clinically atypical encephalitis in boys aged 6 and 8 years. In one case definite evidence of an aetiological relation to the protozoan toxoplasma was found, and there was suggestive evidence in the other. The chief clinical features were generalized convulsions, disorientation, fever, pleocytosis, without such signs of meningeal irritation as nuchal rigidity or Kernig's sign, and absence of signs pointing to involvement of the cranial nerves. One patient died 30 days after onset, and the other recovered.

completely on the tenth day. The chief pathological change in the nervous system was the presence of minute, necrotic, and granulomatous foci.

Putnam, T. J. (1941) *Bull. N.Y. Acad. Med.*, 2 ser., 17, 337.

Sabin, A. B. (1941) *J. Amer. med. Ass.*, 116, 801.

ENDOMETRIOSIS AND ADENOMYOMA

See also B.E.M.P., Vol. IV, p. 561; Cumulative Supplement, Key No. 401; and Surveys and Abstracts 1939, p. 329; 1940, p. 288; and p. 20 of this volume.

Morbid Anatomy and Pathogenesis

Endometrial transplants

In the lungs.—J. E. Hobbs and A. R. Bortnick show that endometrial tissue can be transported from the veins of rabbits to the lungs, in which it remains viable, and invades the parenchyma. They show that implants of uterine and the Fallopian tube mucosae in the lungs may undergo decidual formation if the animal becomes pregnant. The authors conclude that vicarious menstruation is a result of an endometrial implant in whatever region from which the periodic blood discharge issues. Some benign and malignant tumours in the lungs of women may arise from endometrial transplants, and such transplants may be mistaken for tuberculosis.

Clinical Aspects

Treatment

Testosterone propionate.—A woman, aged 28, with endometriosis of the recto-vaginal septum, was treated by L. Wilson with testosterone propionate. The patient refused any treatment which might result in permanent sterility and, as there is evidence that the ovarian cycle can thus be suppressed, Wilson concluded that this ectopic endometrial tissue might also regress under the action of testosterone propionate. There was a large mass in the posterior fornix of the vagina extending from the middle line almost to the right lateral pelvic wall. Intramuscular injections of 50 milligrams of testosterone propionate were given every second or third day for 3 months, then every third or fourth day for a further 10 months. During these 13 months a total of 4,800 milligrams were administered. The first menstrual period after the commencement of treatment occurred at the normal time, but subsequently menstruation was suppressed during the ensuing year. The mucosa of the uterus remained atrophic and the mass in the recto-vaginal septum diminished to one-quarter of its original size. The patient was free from pain throughout. Treatment was finally abandoned owing to undesirable masculinizing effects: the voice became husky, hirsuties resulted, and the clitoris enlarged. Six weeks after the last injection, menstruation started again and thereafter occurred regularly. Pain returned in the rectal region and the tumour started to enlarge again. As a result, the patient has now consented to accept X-ray therapy.

Hobbs, J. E., and Bortnick, A. R. (1940) *Amer. J. Obstet. Gynec.*, 40, 832.

Wilson, L. (1940) *Endocrinology*, 27, 29.

ENDOMETRITIS, CERVICITIS, AND METRITIS

See also B.E.M.P., Vol. IV, p. 574; Surveys and Abstracts 1939, p. 330; 1940, pp. 22 and 288; and p. 20 of this volume.

Cervicitis

Chronic cervicitis

Treatment.—B. Z. Cashman, in a report on the results of deep cauterization in 10,000 cases for the prevention of cancer of the cervix, states that as complete a follow-up as possible found 2 cases only of cancer. Since cancer of the cervix is insidious in its onset, and since chronic cervicitis seems to be an important contributing factor in its aetiology, prevention by adequate treatment of existing cervicitis, and early diagnosis by periodical examination of women over the age of 25, constitute the best solution of the problem. In order to destroy infection in the cervix by cauterization it is often necessary to cauterize deeply and extensively.

According to G. L. Watt, lesions of the cervix should be taken seriously, treated carefully, and watched for signs of malignancy. Cauterization of the cervix is the best treatment for catarrhal inflammation of the cervix, except in very minor cases in which silver nitrate may be used. Amputation of the cervix is the best procedure if there is much hypertrophy or cystic disease. In some cases with lacerations and scarring extending into the vault, with lower abdominal pain, total hysterectomy is the operation of choice.

Cashman, B. Z. (1941) *Amer. J. Obstet. Gynec.*, 41, 216.

Watt, G. L. (1941) *Canad. med. Ass. J.*, 44, 141.

ENTERIC FEVERS

See also B.E.M.P., Vol. V, p. 50; Surveys and Abstracts 1939, p. 330; 1940, p. 289; and p. 63 of this volume.

Typhoid Fever

Treatment

Bananas and nutrition.—W. F. Schoffman finds that banana, especially when supplemented by skimmed milk or butter-milk, is a useful food for the maintenance of nutrition in typhoid patients. It supplies caloric requirements, minerals, and vitamins, and is apparently readily

digestible. After it was given to children with enteric fever the temperature fell strikingly in from 2 to 5 days, though the stools did not show much improvement. The general state of the patients was markedly improved, and the period of acute symptoms was shortened. In the 3 cases treated the stools became negative for typhoid organisms in from 3 to 4 weeks after the onset of symptoms.

Treatment with sulphaguanidine.—J. E. Levi and A. Willen employed sulphaguanidine in a patient who, after a typhoid infection, remained a carrier of *Bacterium typhosum*. The drug was given for 1 week in a dosage of 0.05 gramme per kilogram of body weight every 8 hours. Cultures of the stools taken at various periods thereafter during the next 5 weeks were negative for the organism.

Levi, J. E., and Willen, A. (1941) *J. Amer. med. Ass.*, **116**, 2258.

Schoffman, W. F. (1941) *J. Ped.*, **18**, 399.

EPILEPSY

See also B.E.M.P., Vol. V, p. 96; Cumulative Supplement, Key Nos. 424-432; Surveys and Abstracts 1939, pp. 124, 126, and 331; 1940, p. 291; and p. 91 of this volume.

Aetiology

Cysticercosis

W. Blyth reports a case of cysticercosis epilepsy in a man aged 37 years who had lived in the tropics, and been healthy previously. X-rays of the skull, root of the neck, upper arms, thighs, and legs showed wide-spread evidence of cysticercosis infection. The author believes that the cysticerci, while alive, enjoy a relative tolerance on the part of the host, but that, after their death, they act as foreign irritants and produce changes partly by their toxic effects and partly by increased pressure on surrounding tissues.

Mental and Physical Abnormalities in Epileptics

Benign hyperplasia of the gums

Relation to vitamin C.—The occurrence of swelling, or benign hyperplasia, of the gums has often been reported in epileptics, and according to Kimball is due to vitamin C deficiency caused by treatment with dilantin sodium (sodium diphenylhydantoinate). H. H. Merritt and A. Foster have estimated the vitamin C content of the plasma in many epileptics (altogether 257 patients) treated by dilantin sodium or by phenobarbitone or receiving no treatment, and have reached the following conclusions. The average vitamin C content of the plasma was low in all cases, probably due to deficiency in diet, but there was not any difference between the vitamin C content of the patients treated with dilantin sodium and the others. Moreover, the level of the vitamin C did not bear any relation to the presence or absence of gingival swelling. The ingestions of orange juice or tomato juice by some patients raised the content of vitamin C to 5 times its original level but without any effect on the condition of the gums. The authors therefore conclude that dilantin sodium does not cause vitamin C deficiency nor is such a deficiency the cause of the gum condition.

Treatment

Phenobarbitone and belladonna

In children.—C. E. Schotland and L. H. Loeser treated 12 children with epilepsy with varying doses of phenobarbitone and the laevo-rotatory solanaceous alkaloids in the form of tablets containing phenobarbitone, $\frac{3}{4}$ grain, and the total alkaloids of atropa belladonna, $\frac{1}{100}$ grain. The smallest effective daily dose was $\frac{3}{4}$ tablet, and the largest dose was 6 tablets. In 9 cases there was a marked reduction in the frequency and severity of convulsions. In 2 cases, including one of pyknolepsy, there was no improvement.

Sodium diphenylhydantoinate (dilantin sodium)

Compared with other anti-convulsant drugs.—D. Blair in a critical review on the modern treatment of epilepsy with special reference to sodium diphenylhydantoinate (epanutin, dilantin sodium), and a comparison of its effects with those of other anti-convulsant drugs, such as bromides (lately fallen into disrepute) and luminal (probably the most useful), puts on record his observations on 20 (males 13, females 7) epileptic psychotics of long standing treated for a year by epanutin, and 16 other similar patients thus treated, but for a shorter period. He also summarizes the published reports on this treatment, compares the properties of epanutin with those of other anti-convulsants, and discusses its toxic effects and its true place in the treatment of epilepsy. In his cases females were more benefited than were males, and gained weight, whereas males lost weight; a gain of weight appears to be a good prognostic sign. There was not any correlation between the changes in weight and in blood pressure, blood counts, blood sedimentation rate, or urine. Among the 20 cases 1 only was completely relieved from fits; 6 were greatly, 5 moderately, and 2 slightly improved; 5 unaffected and 1 worse. From a study of the contrasted effects of epanutin and of luminal in 12 of the patients it seems probable that they differ in their power to prevent leptazol fits, this being probably due to some fundamental difference in the way in which they affect the nervous system. A review of the recorded articles shows a wide variation in the estimates of the beneficial effects of epanutin treatment, but confirms the author's opinion of the frequency of toxic symptoms of a nervous nature—subjective, objective, psychological, fever, rashes, hyperplasia of the gums, gastro-intestinal, cardiovascular, rise of blood pressure, and epistaxis. Few fatalities are on record. Very little is known about the mechanism of the

way in which epanutin is such an effective anti-convulsant; it has very little, if any, sedative or hypnotic action. It has been suggested that a combination of epanutin with luminal is more effective than either alone. It remains to be proved that epanutin directly stimulates the cerebral cortex.

Severe toxic effects in the mentally defective.—B. A. M. Williamson, who points out that the amply confirmed anti-convulsant value of sodium diphenylhydantoinate (epanutin, dilantin sodium) may be more than counterbalanced as regards its clinical application on account of the toxic effects, reports a trial series of 20 out of 200 male mental defectives submitted to this form of treatment. Those selected were among the more severe cases of epilepsy, there being approximately equal groups of idiot, imbecile, and feeble-minded patients. The drug was given with all the familiar precautions recommended with its use, and this may explain why so few of the patients showed any early toxic manifestations hitherto described. Severe toxic symptoms occurring 6 weeks or more after the drug was first taken, if hitherto reported, have not been uncompromisingly ascribed to its action. Three comparable reports, however, of this *late toxicity* are quoted by the author—those of A. J. M. Butler, of Weaver, Harrell, and Arnold, and of R. Coope, the last with 2 deaths. Typical late toxicity is thus described: insidious onset with increasing mental dullness; confusion gradually takes the place of dull apathy; lapses from consciousness are preceded by insomnia; constipation is intractable; and retention or oliguria is the rule; an intermittent temperature appears later; and death occurred in 4 cases, in 3 from status epilepticus and in 1 from broncho-pneumonia. Haematoporphyrinuria may occur later, when toxæmia is present. Among oligophrenics, idiots are most prone to toxic manifestations and the feeble-minded less susceptible; imbeciles are in an intermediate position, there being a relation between intolerance and morbid changes. A resemblance between this late toxicity and the effect of nirvanol is pointed out.

Blair, D. (1940) *J. Ment. Sci.*, **86**, 888.

Blyth, W. (1941) *Brit. med. J.*, **1**, 401.

Butler, A. J. M. (1940) *Brit. med. J.*, **1**, 483.

Coope, R. (1939) *Lancet*, **1**, 180.

Merritt, H. H., and Foster, A. (1940) *Amer. J. med. Sci.*, **200**, 541.

Schotland, C. E., and Loeser, L. H. (1941) *Arch. Pediat.*, **48**, 87.

Weaver, O. M., Harrell, D. L., Jun., and Arnold, G. B. (1939) *Virg. med. Mon.*, September.

Williamson, B. A. M. (1940) *J. ment. Sci.*, **86**, 981.

ERUPTIONS, ANOMALOUS AND ATYPICAL

See also B.E.M.P., Vol. V, p. 146; Cumulative Supplement, Key No. 440; and Surveys and Abstracts 1939, p. 334.

Alterations in the Vessels

Familial haemorrhagic telangiectasia

Associated haemorrhages.—H. Alban reports a case of hereditary haemorrhagic telangiectasia in a woman aged 55. Severe nasal haemorrhage began when she was 8 years of age, and had continued at frequent intervals with increasing intensity and with invalidism following the bleeding episodes. The haemorrhages generally occurred without warning and without evident cause, although the patient found that bending often precipitated an attack. For the previous few years there had also been spontaneous haemorrhages from the fingertips, throat, tongue, and ears. There were bleeding tendencies in many other members of the patient's family. The red blood cell count was 3,720,000 and the haemoglobin was 48 per cent. The bleeding time was 2 minutes and 50 seconds and the clotting time 4 minutes.

Hereditary telangiectasia with visceral involvement

Clinical picture.—F. E. McDonough, T. J. Dry, and G. M. Roth report a case of hereditary telangiectasia (Rendu-Osler syndrome) in a man aged 60, with the following unusual manifestations: visceral involvement (presumably a haemangioma of the liver), a cardiac lesion (probably congenital), and a papillary haemangioma of the skin. The patient's mother always had a red face, as did four of his five brothers, four sisters, and a son, but none so red as his. The older members of the family with red faces had, like him, had epistaxis. In cold weather his skin became almost black and he was very intolerant to cold. This intense cyanosis appears to have been associated with cardiac failure. The temperature of the skin was raised as the result of dilated venules and capillaries. There was a bruit over the liver, which was regarded as distinct from the cardiac murmur. The syndrome is defined as a hereditary abnormality characterized by the presence of localized dilatations of small venules or venous terminations of capillaries, chiefly in the skin of the face and the mucosa of the nose, mouth, and gastro-intestinal tract, causing apparently spontaneous haemorrhage, most often recurrent nose bleeding. Various examinations of the blood gave results within the normal limits.

Alban, H. (1941) *Northw. Med.*, *Seattle*, **40**, 86.

McDonough, F. E., Dry, T. J., and Roth, G. M. (1940) *Proc. Mayo Clin.*, **15**, 593.

ERYSIPELAS

See also B.E.M.P., Vol. V, p. 154; and Surveys and Abstracts 1939, p. 335; 1940, p. 297.

Treatment*Sulphanilamide*

J. A. Foley and E. R. Yasuna compared the results of treating 80 cases of erysipelas with sulphanilamide with those of 80 cases which did not receive this treatment. It was found that the patients treated with the drug returned to a normal temperature almost 2 days earlier than the others, that their stay in hospital was shortened by 3 days, that complications occurred twice as often in the control group as in the treated group, and that the mortality rate in the sulphanilamide group was one-fourth that of the untreated group.

Foley, J. A., and Yasuna, E. R. (1940) *J. Amer. med. Ass.*, **115**, 1330.

ERYTHEMA

See also B.E.M.P., Vol. V, p. 159; Cumulative Supplement, Key No. 442; and Surveys and Abstracts 1939, p. 335.

Clinical Picture*Erythema due to external causes*

Livedo reticularis.—N. W. Barker, E. A. Hines, Jun., and W. M. Craig report on 13 cases of a condition characterized by peripheral vascular disease affecting chiefly the legs and feet, which they consider to be cases of livedo reticularis. The condition has been described under other names, such as livedo racemosa, livedo annularis, and asphyxia reticularis. C. M. Williams and H. Goodman divided the cases into three groups: (1) cutis marmorata, (2) livedo reticularis idiopathica, (3) and livedo reticularis symptomatica. In the 13 patients (males 7, females 6) there was no common aetiological factor. Six of the males and 1 female were smokers, 4 were hypertensives. The appearance is that of a mottled, blotchy or reticular bluish discoloration of the skin. There is generally subjective and objective coldness of the skin, the colour of the blotches varying from blue when the patient is in a cold environment, to red or reddish purple when in a warm environment. The persistence of the discoloration, its blotchy distribution, and the extent of the involvement serve to distinguish the condition from Raynaud's disease, and the normal pulsation of the larger arteries distinguish it from thrombo-angiitis obliterans. There are generally organic changes in the arterioles of the skin, with chronic vasospasm, which result in regional atony and dilatation of capillaries and slowing of the blood flow. The condition may be complicated by ulceration of the legs and superficial gangrene of the toes. In 2 of the authors' cases lumbar sympathetic ganglionectomy resulted in some improvement in the circulation.

Erythema due to internal causes

Erythema multiforme.—H. Ageloff reports a case of erythema multiforme bullosum with involvement of the mucous membranes of the eyes and mouth (Stevens-Johnson disease) in a girl aged 4 years. The essential features were, freedom of the scalp, involvement of the mucous membranes of the eyes, mouth, and vagina, an acute course lasting less than 3 weeks, a moderate leucopenia during the first few days of the illness, and complete resolution of the skin lesions with absence of scar formation.

Erythema nodosum associated with tuberculosis.—A. L. Punch reports 3 cases of erythema nodosum in young adults with a persistently negative Mantoux test which ultimately became positive, thus showing the presence of primary tuberculous infection; coincident with this primary infection erythema nodosum appeared in all 3 patients. The author concludes that in these cases the erythema nodosum was a manifestation of tuberculous infection.

Erythema scarlatiniforme.—A. L. Hoyne and L. R. Leviton report 6 cases of a symptom-complex with a scarlatiniform eruption. The members of this group were in close contact with one another. Although a common aetiological factor could not be established for all the patients, the condition appears to be contagious. Repeated blood-agar cultures for haemolytic streptococci were negative, and blanching tests for scarlet fever were also negative. All patients had fever, leucocytosis, and pharyngitis, and all the infants a profuse nasal discharge.

O. E. Billo records 8 cases of mercurial erythema in young men which were first diagnosed as scarlet fever. The patients were shown to have rubbed the skin with blue mercurial ointment (93 per cent mercury) for relief of pediculosis. The systemic reactions appeared about 5 days after contact with mercury and the rash lasted about a week, and desquamation, often fine and limited in extent, occurred in every patient. The Dick, Schultz-Charlton, and Wassermann tests were negative, the leucocyte count was not raised, β -haemolytic streptococci were not found in the throat and in all but one the temperature was raised to 101° F. or over. The author quotes with approval from a forgotten London physician, G. Alley, who more than a century ago described three classes of these cases as (1) hydrargyria mitis, without fever, but with headache and nausea and with or without desquamation; (2) hydrargyria simplex, with fever, 102°–106° F., headache and usually sore throat (at first it may resemble German measles and when on the decline closely simulates scarlatina anginosa); and (3) hydrargyria maligna, with prominent sore throat. The colour of the eruption is dark, sometimes almost purple; vesicles of large size and large flakes of desquamation occur and the nails of the fingers and toes may be shed.

- Ageloff, H. (1940) *New Engl. J. Med.*, **223**, 217.
 Alley, G. (1810) *Observations on the Hydrargyria or that Vesicular Disease arising from the Exhibition of Mercury*, Lond.
 Barker, N. W., Hines, E. A., Jun., and Craig, W. M. (1941) *Amer. Heart J.*, **21**, 592.
 Billo, O. E. (1941) *Amer. J. med. Sci.*, **201**, 756.
 Hoyne, A. L., and Leviton, L. R. (1941) *Arch. Pediat.*, **58**, 69.
 Punch, A. L. (1941) *Lancet*, **1**, 10.
 Williams, C. M., and Goodman, H. (1925) *J. Amer. med. Ass.*, **85**, 955.

ERYTHRAEMIA

See also B.E.M.P., Vol. V, p. 176; and Surveys and Abstracts 1939, p. 336; 1940, p. 297.

Clinical Picture

Thrombosis

Causes and treatment.—L. Stover and W. E. Herrell report a case of a man, aged 66, with erythraemia complicated by extensive thrombosis of the right subclavian and axillary veins, associated with thrombophlebitis and lymphoedema, and review the recorded examples of vascular thrombosis in erythraemia, involvement of the upper limbs being rare. Three years earlier the patient had had thrombophlebitis in the right thigh followed by bilateral pulmonary embolism. In the second attack the veins of the right axilla and anterior chest wall were extremely enlarged and there was a maculo-papular eruption all over the body, excepting the legs and face, which he called 'prickly heat'. The red cells numbered 7,420,000, leucocytes 14,300 per cubic millimetre. Phlebotomy was performed and in the course of 9 days 6,000 cubic centimetres, or more than 90 per cent of the total blood volume of a normal person of the same weight as the patient, was removed. A good recovery was made, the patient being advised to continue phenylhydrazine treatment. N. W. Barker, also of the Mayo Clinic, mentions as causes of thrombophlebitis in erythraemia: infective foci, recent operation or intravenous injections, other injury to veins, and increased viscosity of the blood. The most satisfactory treatment for erythraemia is daily venesections until the volume of blood and the concentration of erythrocytes are reduced to within normal limits. The average patient with erythraemia requires 0.3 gramme phenylhydrazine hydrochloride once a week.

Adjustment of the circulation

H. J. Stewart, C. H. Wheeler, and N. F. Crane report on the circulatory adjustments, such as the cardiac output, oxygen consumption, cardiac size, left ventricular work, and other related functions in 6 patients with erythraemia. When the amount of haemoglobin and the red cell count were increased above normal, the arteriovenous oxygen difference was increased, the cardiac output per beat and the cardiac index were decreased, and the oxygen content of both the arterial and venous blood was increased. There was no consistent variation from normal in the left ventricular work, cardiac size, basal metabolic rate, blood pressure, and other functions of the circulation. When, as a result of treatment, a reduction of the level of the haemoglobin and red blood cells occurred, the arteriovenous oxygen difference decreased and the cardiac index and output per beat increased and attained normal values when the red blood cells reached normal levels. There was a linear relation between the amount of haemoglobin and the number of red blood cells on the one hand and the cardiac output and the cardiac index on the other.

Treatment

Lipocaiac and choline

'Experimental polycythaemia', persistent increase in the circulating erythrocytes, can be produced, according to some authors, by administration of cobalt, exposure to reduced oxygen tension, and exercise, and it is claimed that such polycythaemia can be controlled or prevented by raw liver given orally, by certain liver extracts given orally and by injection, and by feeding with choline hydrochloride. On the basis of these reports G. Carpenter tested the effects on 4 patients, diagnosed as the subjects of erythraemia, of choline hydrochloride and lipocaiac, the pancreatic hormone with an action similar to, but much more intense than, that of choline on lipid metabolism. The dosage of choline hydrochloride was 0.6 gramme 3 times daily, and of lipocaiac 12 capsules of approximately 10 grains each, daily. One patient received choline hydrochloride only, 1 lipocaiac only, and the other 2 had first choline hydrochloride and subsequently lipocaiac. Neither drug had any effect on the erythrocyte count over periods of up to 1 month.

Vitamin C

J. Deeny, in a review of the relation of vitamin C to erythraemia, records 2 cases which showed that vitamin C alone had little effect on the condition, but, in conjunction with sodium bicarbonate, improved the general health and was followed by a marked fall in the red cell count and by diuresis. The dosage was 400 milligrams daily of vitamin C and 1 ounce of sodium bicarbonate.

- Barker, N. W. (1940) *Proc. Mayo Clin.*, **15**, 821.
 Carpenter, G. (1940) *Amer. J. med. Sci.*, **200**, 462.
 Deeny, J. (1940) *Brit. med. J.*, **2**, 864.
 Stewart, H. J., Wheeler, C. H., and Crane, N. F. (1941) *Amer. Heart J.*, **21**, 511.
 Stover, L., and Herrell, W. E. (1940) *Proc. Mayo Clin.*, **15**, 817.

ERYTHROCYANOSIS

See also B.E.M.P., Vol. V, p. 183.

Clinical Picture*Adiponecrosis e frigore*

Due to intense cold.—H. Haxthausen describes as a peculiar affection of the subcutaneous adipose tissue of the face, *adiponecrosis e frigore*, appearing after exposure to intense cold. The affection consists of hard, well-defined infiltrations which clinically and histologically resemble those in *adiponecrosis neonatorum*. Of the author's 5 cases, 4 were in very young children. One in a young woman was associated with ordinary frost-bite and *pernio*. The disorder has a benign course, disappearing spontaneously in a few weeks.

Treatment*Acrocyanosis*

Cervico-thoracic sympathectomy.—N. W. Barker and G. S. Baker report a case of the comparatively rare vascular disease *acrocyanosis* (*erythrocyanosis*) of 10 years' duration in a woman aged 41. As a diagnostic procedure 20 cubic centimetres of 1 per cent metycaine (the hydrochloride of α -(2-methyl piperidino)-propyl benzoate) was injected into the left cervico-thoracic sympathetic ganglia. The patient was then placed in an environment temperature of 5° C. The fingers and hand of the right side became deeply cyanotic, the skin temperature of the fingers on the right side falling to 16° C., whereas the left hand and fingers remained pink and the temperature of the skin there was 33.9° C.; the left upper extremity was free from pain. These results indicated that cervico-thoracic sympathetic-ganglionectomy should be beneficial; this was carried out with success. It is fairly well established that arteriolar spasm is the basis for the physiological disturbance in *acrocyanosis*, the capillary dilatation being secondary and due to atony, and not to venous obstruction. Some definite differences between the discoloration in the following circulatory disorders affecting the extremities and causing cyanosis, are worthy of note:

	COLOUR CHANGES		RAYNAUD'S DISEASE	ACROCYANOSIS	LIVIDO RETICULARIS
Location	—	—	— Fingers and toes	Hands, fingers, feet, and toes	Legs, feet, toes, arms, hands, and fingers
Extremities with maximal involvement	—	—	Upper extremities	Upper extremities	Lower extremities
Character	—	—	Diffuse	Diffuse	Reticular or blotchy
Time	—	—	Intermittent	Constant	Constant
Blanching	—	—	Intermittently present (first phase)	Absent	Absent

Barker, N. W., and Baker, G. S. (1940) *Proc. Mayo Clin.*, **15**, 601.

Haxthausen, H. (1941) *Brit. J. Derm.*, **53**, 83.

ERYTHROMELALGIA

See also B.E.M.P., Vol. V, p. 188; and Surveys and Abstracts 1939, p. 337.

Symptoms and Signs*With review of diagnosis and treatment*

E. D. Telford and H. T. Simmons point out that since S. Weir Mitchell described in 1878 redness and burning pain of the extremities under the title of *erythromelalgia*, and regarded it as a vasomotor neurosis, so much confusion has arisen on account of the frequency with which redness and pain are combined in disorders of the peripheral circulation. Accordingly some authors have come to the conclusion that it is not a separate disease but a group of symptoms. Telford and Simmons, however, regard the condition as a separate entity, but as very rare, for during 9 years in a busy neurovascular clinic they have accepted 4 examples only. Painful rubor is the condition which superficially resembles *erythromelalgia* and has caused most of the existing confusion. It is common in some peripheral vascular diseases, and is not painful in the early stages, though in later phases pain becomes constant, 'a rest pain'; it is relieved by the dependent position, and on elevation the redness disappears and its place is taken by pallor, thus differing from *erythromelalgia*. Treatment in the past has been purely symptomatic and of little avail. As *erythromelalgia* is probably due to some disorder of the sympathetic system it appeared justifiable to perform bilateral cord ganglionectomy; this was carried out in 3 of the 4 patients with excellent results, the pain disappearing at once and not returning.

Telford, E. D., and Simmons, H. T. (1940) *Brit. med. J.*, **2**, 782.

EYE EXAMINATION

See also B.E.M.P., Vol. V, p. 216; and Surveys and Abstracts 1939, p. 337.

Routine Examination*Cornea*

Use of fluorescein in various conditions.—H. Gifford employs intravenous injections of 10

cubic centimetres of a 10 per cent solution of sodium fluorescein as a means of studying the circulation of the aqueous in clinical cases. The method is non-toxic and produces no unpleasant symptoms in the patient. In the normal eye fluorescein appears in about 3 minutes. The time of appearance and the concentration of the dye are definitely diminished in keratoconus. This suggests the use of parasympathetic-stimulating drugs in the treatment of this condition. This test may also be of value in establishing the diagnosis of early keratoconus. It is of value in proving the presence and position of vitreous in the anterior chamber, and for selecting the site of a filtering operation for glaucoma after cataract extraction. It may prove of value in separating the secretory from the purely obstructive type of glaucoma.

Fundus

Importance of reflexes.—In a presidential address to the Ophthalmology section of the Royal Society of Medicine, A. J. Ballantyne discussed the importance of reflexes of the fundus oculi as an indication of the texture and structure of the reflecting surfaces, and in the recognition of pathological conditions in the underlying tissues. For the most satisfactory biomicroscopic examinations of physiological reflexes, long and short wave-lengths by means of sodium and mercury vapour lamps should be used, together with ophthalmoscopic lights; and the subjects examined should be young, with good pigmentation, and the pupils should be undilated and with emmetropic refraction. Surface reflexes disappeared in the light of the sodium lamp and thus the changes in the deep layers of the retina and choroid were clearly seen. Several physiological reflexes could be observed on the surface of the internal limiting membrane. These were the perimacular halo, the fan reflex in the macular depression, foveal pit reflexes, and the patchy reflexes. The patchy (or 'watered silk') reflexes were usually lightly striated in correspondence to the nerve fibre striations or had a granular or latticed appearance. Reflexes of different appearance, for example, 'beaten metal' reflexes, those formed on the hyaloid membrane (so-called) and flaked or dotted surface reflexes, were probably all pathological, with the exception of Gunn's dots, which were truly physiological. Punctate reflexes in the centre of the fundus indicated degeneration of the retinal pigment and resulted from retino-choroiditis or severe retinitis. It is suggested that they indicate the presence of highly refractive substances in the retinal exudate or in another lesion. The existence of physiological linear reflexes was uncertain. Pathological linear reflexes took various forms; linear reflexes associated with traction folds appeared in the presence of choroido-retinal scarring, or cystic degeneration of the macula or of a macular hole. Annular reflexes usually indicated elevations or depressions of the retina, for example, a tumour. Reflexes associated with pressure folds indicated orbital cysts; abscesses or neoplasms and the needle-shaped, broad linear, or Vogt reflexes, were associated with papillo-retinal oedema. Retinal folds may occur without surface reflexes, indicating a corresponding folding of the internal limiting membrane, and linear reflexes may occur without retinal folds. In the normal fundus, especially in a brunette, a mirror reflex from the pigmented epithelial layer might sometimes be seen. Granular, crystalline reflexes from the external limiting membrane or the pigmented epithelium often indicated senility or retino-choroidal degeneration or trauma; they were sometimes anterior to the retinal vessels. Pathological reflexes tended to disappear and reappear and change from one form to another, according to the pathological condition of the eye, and might finally become physiological reflexes.

Ballantyne, A. J. (1940) *Proc. R. Soc. Med.*, **34**, 19.

Gifford, H. (1940) *Arch. Ophthalm.*, N.Y., **24**, 122.

EYELIDS, INJURIES AND DISEASES

See also B.E.M.P., Vol. V, p. 239; and Surveys and Abstracts 1939, p. 338; 1940, p. 298.

Inflammation

Blepharitis

Treatment with brilliant green.—A. G. Franks treated 12 patients with non-ulcerative blepharitis by the application of brilliant green (tetraethyl-diaminotriphenylmethane sulphate). Some of the lesions were associated with seborrhoeic dermatitis, acne, or sycosis vulgaris, and others were of unknown aetiology. The duration was from 2 weeks to 4 years. The solution was applied to the eyelids daily for several weeks with a small applicator so as not to stain the surrounding skin unnecessarily. There were not any ill effects from contact of the solution with the conjunctiva. The patients wore smoked glasses to avoid attracting attention. The stain wore off within a few days after ceasing treatment. In all patients the condition cleared up entirely, or greatly improved. After a year there was no recurrence.

Treatment with gentian violet and brilliant green paste.—A. T. Elder reports that in a total school population of 7,317 there were 68, or about 1 per cent, cases of chronic blepharitis. These were classified into two groups: a mild type, characterized by flaky incrustations on the lid margins, slight swelling of the lids, but without ulceration—the squamous type; and a severe form characterized by small ulcers at the roots of the eye-lashes, swollen and discoloured lid margins, destruction of lashes, and occasionally conjunctivitis of the ulceration type. Of the 68 cases, 44 children attended the clinic for treatment for a period of 8 weeks. Treatment consisted of the application, morning and night, to the roots of the eyelids, after removal of crusts with boric acid lotion, of a paste consisting of gentian violet 0.5 per cent, brilliant green 0.5 per cent, and wool fat to 100. Of 37 cases of the squamous type all the

children were free from symptoms after 8 weeks, but in the ulcerative cases there was little or no improvement. In these severe cases, after preliminary cleansing with hydrogen peroxide solution, an aqueous solution of gentian violet may be applied.

Elder, A. T. (1940) *Brit. med. J.*, **2**, 185.

Franks, A. G. (1941) *Arch. Ophthalm., N.Y.*, **25**, 334.

FALLOPIAN TUBES DISEASES

See also B.E.M.P., Vol. V, p. 250; Surveys and Abstracts 1939, p. 338; 1940, pp. 23 and 298; and p. 20 of this volume.

Infections

Gonorrhoeal salpingitis

Oestrogenic therapy.—According to G. Weitzner there is a 'danger period' at the time of menstruation when attacks of gonorrhoeal salpingitis are likely to occur or recur. It was found that 30,000 international units of oestrogenic hormone, divided into 3 doses and given intramuscularly at 3 daily intervals with the onset of menstruation, successfully bridged over this 'danger period'. Injection of 10,000 international units is recommended at frequent or daily intervals in the treatment of acute gonorrhoeal salpingitis, and satisfactory results are reported from this treatment in 74 cases of chronic, and 91 cases of acute, salpingitis during a period of 30 months.

Tumours of the Fallopian Tubes

Primary carcinoma

H. A. Baron gives an account of primary carcinoma of the uterine (Fallopian) tubes, based on 365 cases. The usual origin of the growth is in the outer two-thirds of the tube, and in approximately a third of the cases both tubes are affected. Microscopically, three forms of carcinoma have been described: (1) malignant papilloma, the commonest, (2) malignant adenoma which by spreading into the body of the uterus may imitate a primary growth of the fundus, (3) alveolar carcinoma, thought to be due to fusion of the papillae in (1). Forms (1) and (3) may occur in the same tube. The alveolar carcinoma may be squamous-celled and even show epithelial pearls. Clinically pain may at first be referred to the upper abdomen and may be gastro-intestinal, but the commonest symptoms are abdominal, vaginal discharge, and vesical pain. No symptoms, however, are pathognomonic, because adnexal disease, uterine fibromyoma, and ovarian cysts are often present. One case only has been correctly diagnosed before operation. As diagnosis is so difficult and made late, the prognosis is bad. Treatment consists in panhysterectomy, bilateral salpingo-oophorectomy, removal of infected lymphatic glands if possible; in every case X-ray treatment should follow operation.

Diagnosis.—K. H. Martzloff reports a case of primary carcinoma of the Fallopian (uterine) tube. The manifestations of this comparatively rare condition are so protean, and in general so similar to other types of adnexal disease, that there is little logical basis for suspicion of its presence. A tentative diagnosis, however, may be made in that limited group of patients with the syndrome of *hydrops tubae profluens* with a sero-sanguineous vaginal discharge, but no causal vaginal or uterine pathology.

Origin in uterus

Cancer particles.—O. Wallis, reviewing previous reports, finds that the occasional discovery of free and implanted cancer particles in the Fallopian (uterine) tubes in cases of uterine and ovarian cancer is not as uncommon as was formerly believed. Cancer cells and particles may enter the Fallopian tubes by either or both ends. The author reports a case of a typical adenocarcinoma of the body of the uterus associated with a secondary growth in the posterior cul-de-sac. Pieces of the tumour were found free in the lumen of the left tube near its fimbriated end.

Tubal Pregnancy

Aetiology

Pre-existing tubal infection.—From analysis of 73 cases of tubal pregnancy, K. W. Woodhouse supports the view that pre-existing tubal infection is an important cause of ectopic gestation; in 65.8 per cent of the 73 cases there was a definite history or evidence of pelvic inflammation. The incidence was highest between the ages of 25 and 35, or 52.1 per cent of the 73 cases. The average married period was 9.74 years, and 78.6 per cent of these women had been pregnant on an average of 2.83 occasions. The mortality rate in the series was 1.37 per cent.

Differential diagnosis

R. L. Dodds analyses 40 personal cases seen during 3 years. There were 14 nulliparae, 2 of whom had had gonorrhoea and 1 a pelvic abscess. Among the 26 parous patients 20 had borne a child, 6 had had miscarriages, and also in 6 a previous pelvic operation had been performed. In no case was there a history of insufflation of the tubes, a procedure regarded by the author as 'almost as fertile of extra- as of intra-uterine pregnancy'. The difficulties of correct diagnosis are considerable; among the cases seen by the author and diagnosed as extra-uterine pregnancy, there were 6 cases (not included in the 40 cases), 4 of these being acute salpingitis, 1 threatened miscarriage, and 1 of herpes zoster. Among 36 cases sent in with some kind of diagnosis 7 were correct and 29 wrong. One reason for this failure of correct recognition is the rarity of extra-uterine pregnancy as compared with salpingitis,

acute appendicitis, and miscarriage for which it is commonly mistaken. Although amenorrhoea is a valuable positive sign, it was recorded in half only of the 40 cases. There are two categories of ectopic gestation: acute (19) and subacute (21) cases. The mistaken diagnosis of appendicitis is seldom fatal, as the operation is usually carried out at an early stage; the author has not seen an extra-uterine gestation starting with peri-umbilical pain and vomiting. Acute salpingitis is not a surgical condition, and a case so diagnosed in which 4 days' efficient medical treatment is not followed by improvement is probably one of ectopic gestation. There was 1 case of probable bilateral tubal pregnancy. Two cases proved fatal, both on the operating table. Much stress is laid on pain in the shoulders, and its presence in a woman with an acute abdomen is regarded as pathognomonic of ectopic gestation.

Baron, H. A. (1940) *Canad. med. Ass. J.*, **43**, 118.

Dodds, R. L. (1940) *Proc. R. Soc. Med.*, **33**, 783.

Martzloff, K. H. (1940) *Amer. J. Obstet. Gynec.*, **40**, 804.

Wallis, O. (1941) *Amer. J. Obstet. Gynec.*, **41**, 196.

Weitzner, G. (1941) *Amer. J. Obstet. Gynec.*, **41**, 92.

Woodhouse, K. W. (1940) *Amer. J. Surg.*, **49**, 3.

FIBRILLATION, MUSCULAR

See also B.E.M.P., Vol. V, p. 276.

Aetiology

In nervous diseases

Peripheral origin.—From observations on a volunteer, an elderly man with amyotrophic lateral sclerosis and generalized fibrillary twitches in both lower extremities, C. H. Shelden and H. W. Woltman of the Mayo Clinic are of opinion that muscular fibrillation in diseases such as progressive muscular atrophy, progressive bulbar paralysis, and amyotrophic lateral sclerosis, is due to some alteration in the response of the neuromuscular unit at its periphery, presumably to a chemical agent, and not to irritation or degeneration of the more central cells in the anterior horn of the spinal cord. In the patient mentioned above and also in another patient with amyotrophic lateral sclerosis, it was shown that after complete motor and sensory paralysis had been induced by the administration of 70 milligrams of procaine in 2 cubic centimetres of cerebrospinal fluid, biopsy of one gastrocnemius muscle, and clinical examination of other muscles while anaesthesia persisted, fibrillation remained unchanged. Attention is drawn to the observations on the diseases mentioned above, by D. Denny-Brown and J. B. Pennybacker, showing that in the explanation of fasciculation at least some activity of the nerve fibre or the cell in the anterior horn of the spinal cord is necessary.

Denny-Brown, D., and Pennybacker, J. B. (1938) *Brain*, **61**, 311.

Shelden, C. H., and Woltman, H. W. (1941) *Amer. J. med. Sci.*, **201**, 884.

FIBROSITIS

See also B.E.M.P., Vol. V, p. 279; Cumulative Supplement, Key No. 489; and Surveys and Abstracts 1940, p. 299.

Diagnosis and Differential Diagnosis

Idiopathic myalgia

Myalgic spots.—M. Gutstein-Good states that idiopathic myalgia is characterized by the presence of myalgic spots causing referred pain which may simulate visceral or other diseases. For example, myalgia of the pectoralis major muscle may cause precordial pain, myalgia of the lumbar or thigh muscles sciatica or neuralgia in the testes or groin, myalgia of the arm muscles pain in the forearm and hand, and myalgia of the trapezoid muscles vertigo. The injection of 2 cubic centimetres of a 1 per cent solution of procaine into the myalgic spots, which are well-defined areas situated at the origin or insertion, along the edge, or in the course of a muscle, and pressure on which elicits an agonizing pain, may lead to a lasting cure.

Treatment

Physical methods

Heat and Scott's dressing.—T. H. Howell shows that among the 400 in-pensioners of the Royal Hospital, Chelsea, nearly all 65 or more years of age, 35, or 11.4 per cent, suffered from any of the various forms of rheumatic disease during the year October 10, 1939–October 10, 1940. Fibrositis with 24 patients headed the list and osteoarthritis with 6 came next. This runs counter to the usual impression that rheumatism is common in old age. These pensioners have advantages in the regular community life, the warm uniform provided, the ample diet with adequate vitamins and calories, a daily visit from a nurse, and a weekly inspection by the medical officer. At first fibrositis was treated by heat alone or with deep massage. Ung. methyl salicyl. gave good results; but Scott's dressing (ung. hydrarg. co.) when well rubbed in under the heat of the infra-red lamp, and the excess wiped off, proved far the most successful method and became the routine; 10 patients thus treated recovered after 5 treatments or less; all of these were over 70 and 2 more than 80 years of age.

General

Injection of local anaesthetic.—M. Button claims rapid restoration of function by injection of a local anaesthetic in muscular rheumatism, that is such conditions as stiff neck, lumbago, pseudo-sciatica, deltoid rheumatism, and traumatic types of rheumatism, for example, 'tennis

elbow', 'painful heel', and 'pectoral pain'. Injections are given into the muscle, about $\frac{1}{2}$ inch beneath the surface of the fascia covering the muscle, at the point of maximal tenderness on deep pressure. Through a single skin puncture 0.5 cubic centimetre of a 2 per cent solution of novocain with adrenaline is injected in several directions through separate punctures in the fascia. If there is more than one area of tenderness, several injections may be necessary.

Diet

Vitamin E.—Reports show experimental evidence of the importance of deficiency of vitamin E in the causation of muscular disease, and of the clinical benefit from its use in primary muscular dystrophias, amyotrophic lateral sclerosis, acute poliomyelitis, and after multiple neuritis. C. L. Steinberg treated 82 patients with wheat-germ oil, 2 to 8 cubic centimetres daily. All the patients had previously received other treatment for 3 months to 2 years. The conditions so treated were as follows: (1) Primary fibrositis, 30 cases; the author admits that few medical men recognize this form, and states that it may masquerade under the titles of lumbago, torticollis, myositis, and panniculitis; all these patients were completely cured. (2) Fibrositis due to rheumatoid (atrophic) arthritis: 8 of the patients were improved and 12 not benefited. (3) Osteoarthritis (hypertrophic arthritis), 20 cases; no benefit in the soft tissues. Eight psychoneurotic patients were all resistant to the treatment. Thus the treatment of secondary fibrositis is disappointing. It is suggested that primary fibrositis may be a metabolic rather than an infective process.

Button, M. (1940) *Brit. med. J.*, **2**, 183.

Gutstein-Good, M. (1940) *Lancet*, **2**, 326.

Howell, T. H. (1941) *Brit. J. Phys. Med.*, N.S. **4**, 37.

Steinberg, C. L. (1941) *Amer. J. med. Sci.*, **201**, 347.

FLUKE INFECTIONS, INTESTINAL

See also B.E.M.P., Vol. V, p. 320; and Cumulative Supplement, Key Nos. 496–502.

Fascioliasis

Treatment

Fasciola hepatica removed from common bile-duct.—P. Manson-Bahr and J. Walton record the successful removal of *Fasciola hepatica* from the common bile-duct of a woman, aged 54, who had never been out of Great Britain, and had undergone cholecystectomy and 7 years later was operated upon and the fluke found in a dilated common duct. This like the previous operation was followed by relief, but the symptoms returned. The faeces did not contain ova, but the possibility of infestation still remained. A list of 10 British cases is given, including the case reported by R. C. Clark who found the parasite while operating on a suppurating gall-bladder, the only previous case of surgical removal. The medical treatment, which is admittedly unsatisfactory, is discussed, especially the intravenous injection of emetine hydrochloride, carbon tetrachloride by the mouth, and gentian violet 1 per cent intravenously. A more heroic suggestion is that the parasites should be forced out of the gall-bladder by open surgical drainage for 2 to 3 weeks, as recommended by K. Burgi.

Manson-Bahr, P., and Walton, J. (1941) *Brit. J. Surg.*, **28**, 380.

FOETUS DISEASES, MALFORMATIONS AND MONSTROSITIES

See also B.E.M.P., Vol. V, p. 334; Cumulative Supplement, Key Nos. 503–512; and Surveys and Abstracts 1939, p. 340; 1940, p. 301.

Abnormal Conditions in Living Foetus

Skin

Ehlers-Danlos syndrome.—H. S. Barber, J. Fiddes, and T. H. C. Benians contribute a review of the history and details of the syndrome described first by Ehlers in 1899 and expanded by Danlos in 1908. It consists of the triad (1) over-extensibility of the joints, (2) over-elasticity of the skin, and (3) friability and vulnerability of the skin to injury. To these F. P. Weber added a less constantly recognized change in the subcutaneous tissues, freely movable nodules, and spherules of fat. The authors record 2 cases and pay much attention to the histological appearances. Much interest is attached to the pseudo-tumours; apart from the fatty spherules, they show two types both due to trauma. In their first case an inflammatory granuloma formed around an implantation dermoid cyst. The giant cells in this inflammatory tissue bore some resemblance to proliferated sweat glands. In their other case the tumour appeared to arise from two causes: (1) the absence of elastic tissue in the injured area which allowed bulging, and (2) the presence of large pale swollen bundles of collagen. The aetiology is obscure, but the basis is probably a developmental defect; congenital cases occur, and in these the diagnosis may be facilitated by another sign, viz. absence or delay of cranial ossification. Although there is some doubt about the hereditary and familial basis, there is a considerable accumulation of evidence in favour of an hereditary factor.

Partial onychia (recessive) with bony changes.—N. M. Jacoby, H. A. Ripman, and J. M. Munden report a case of partial onychia (recessive) with hypertrophy of the gums and multiple osseous abnormalities in a girl aged $2\frac{1}{2}$ years. The case appeared to be a combination of two extremely rare congenital abnormalities with additional defects of the bones. The face showed slight hypertelorism, rudimentary epicanthic folds, and, with bulging gums, gave her an appearance suggesting mental deficiency, but this was not confirmed by mental

tests. The parietal bones showed bossing and a depression was palpable in the position of the anterior fontanelle, but radiologically the bones were united. The lower incisors were the only teeth erupted and elsewhere there was much swelling of the alveolar margins. Radiologically the teeth were present in normal numbers. In the hands the 5th fingers on both sides were short and the terminal phalanges inverted. The nails were completely absent from both thumbs and 5th fingers and from the left ring finger. In the feet all the toe nails, except the right 2nd toe, were absent. The skeletal changes showed (1) precocity of ossification of all bones, the appearances being those of a child 4 to 6 years old; (2) maldevelopment of the terminal phalanges of the hands and feet; and (3) maldevelopment of the vertebrae.

Digestive system

Congenital obliteration of bile-ducts.—M. J. Smyth records the above condition in a female infant, 6 months old at the time of death, who had been jaundiced since birth. Although the author had found records of congenital obliteration of the bile-ducts associated with transposition of some viscera, he had not found one of total transposition (*situs inversus*). At the necropsy the common bile-duct could not be found, the cystic duct was a fibrous cord, and the gall-bladder was represented by a thin-walled cyst, the size of a tangerine, containing clear greenish-yellow fluid. The remains of the cystic duct did not join the gall-bladder. There were 22 splenunculi.

Triplication of the colon.—A. W. Gray reports a case of triplication of the large intestine in an infant who died at the age of 11 months. Cases of double intestine have been reported, but this appears to be the first case of triplication noted. At necropsy it was found that the colon was in the usual site, but was markedly dilated and, at the recto-sigmoid junction, it ended in a cul-de-sac. Posterior and just superior to the ileocaecal valve were two small apertures which opened freely into two completely distinct undilated tubes which lay in the posterior and medial walls of the dilated blind channel. These two colons passed into a single rectum. The patient showed many other congenital abnormalities.

Genito-urinary system

Relation to chronic pyuria.—In a paper on congenital anomalies of the urinary tract in children and infants and their relation to chronic pyuria I. H. Erb and P. Summerfeldt report that among 1,148 necropsies there were 51, or 4.4 per cent, of these anomalies as compared with 117, or 2.4 per cent of such anomalies among 4,903 necropsies recorded in 1924 by H. G. Bugbee and M. Wollstein. In addition to the 51 cases there were 7 cases of hydro-ureter and hydronephrosis without any organic congenital abnormality. Sixty-seven per cent of these cases occurred in infants under 1 year of age, and males were twice as often attacked as females. Although congenital anomalies may occur in any part of the urinary tract, the most important were those of the valves in the posterior urethra in boys, stenosis at the uretero-vesical or uretero-pelvic (renal) junctions, and abnormal renal arteries, as they are prone to cause obstruction, urinary stasis, compression atrophy of the renal elements, hydronephrosis, infection, and pyuria. Horse-shoe kidney may be latent and found after death from other causes, but the anterior position of the ureters in front of the bridge of renal tissue connecting the two lower poles exposes them to more risk of compression and resulting hydronephrosis and subsequent pyuria, than in normal persons. Among the 51 cases there were 33 congenital anomalies in other parts of the body. Morbid structural changes—hypertrophy and trabecularization of the urinary bladder, hydro-ureter, with ureteral angularity, hydronephrosis and hydronephrotic compression-atrophy—in 26 cases were ascribed to obstruction, in 4 cases to neuro-muscular dysfunction, and in 3 cases the cause was not determined.

According to M. F. Campbell, ureterocele is a congenital obstructive lesion in which secondary urinary infection is the important complication. The resulting persistent pyuria, too often called chronic pyelitis, is the symptom which almost always calls for the urological diagnostic investigation. The clinical picture is almost always that of 'chronic pyelitis', and urinary back-pressure pain may be prominent. The diagnosis is readily made by urological examination. The immediate treatment is removal of the obstruction. The essential accessory therapy is eradication of urinary infection, calculi, or other complicating lesions.

Monorchia.—V. S. Counseller, D. R. Nichols, and H. L. Smith report 7 cases of monorchia. In 4 cases the absence of the testis occurred on the left side, and in 3 on the right. A study of these cases did not reveal any conclusive evidence as to the cause of the condition, nor did it indicate any diagnostic physical signs as an aid in differentiating anorchidism from cryptorchidism.

Barber, H. S., Fiddes, J., and Benians, T. H. C. (1941) *Brit. J. Derm.*, **53**, 97.

Bugbee, H. G., and Wollstein, M. (1924) *J. Amer. med. Ass.*, **83**, 1887.

Campbell, M. F. (1941) *J. Urol.*, **45**, 598.

Counseller, V. S., Nichols, D. R., and Smith, H. L. (1940) *J. Urol.*, **44**, 237.

Erb, I. H., and Summerfeldt, P. (1941) *Canad. med. Ass. J.*, **44**, 14.

Gray, A. W. (1940) *Arch. Path.*, **30**, 1215.

Jacoby, N. M., Ripman, H. A., and Munden, J. M. (1940–41) *Guy's Hosp.*

Rep., **90**, 34.

Smyth, M. J. (1941) *Brit. med. J.*, **1**, 84.

FOOD

See also B.E.M.P., Vol. V, p. 388; and Surveys and Abstracts 1939, p. 341; 1940, p. 301.

Major Constituents of Food*Nitrogenous constituents*

Supplementary amino-acids in diet.—I. S. Klieger investigated the amino-acid content of the average diet. He concludes that the hypothesis in favour of the use of a mixture of amino-acids to supplement the average diet, as well as the reducing diet, is well supported by clinical evidence. In 20 children who were at least from 5 to 20 points underweight, 10 showed a clear gain in weight and appetite after being given a mixture of amino-acids. Of 10 adults similarly treated, 8 showed a substantial improvement in weight, 1 patient gaining as much as 14 pounds in 5 weeks.

Inorganic Salts*Calcium*

Abundance in present-day diets.—I. Harris, J. T. Ireland, and G. V. James state that there is no evidence that the vast majority of the population of this country are suffering from the effects of calcium insufficiency. The calcium intake under the present dietary régime, indeed, appears to be ample. On the other hand evidence exists that large sections of the community take too much of the type of food rich in calcium. Although there may therefore be some reason for reduction of the food calcium, there is not any for increasing it.

Food Requirements and Intakes*Minimum optimum requirements*

Simple dietaries.—L. Hill points out that millions of Russians live on black bread and cabbage soup, but could not live on white bread or on the 'fortified' white bread of the Ministry of Food. Millions in Tibet and Sinkiang live on parched barley and buttered tea, and rickshaw runners in Japan can run 50 miles in a day on a diet of rice, salads, and a little fish. From these and other examples, the lesson therefore is that we can give up very much of our accustomed diet, and if necessary live on very simple food without any detriment to our health.

Harris, I., Ireland, J. T., and James, G. V. (1941) *Brit. med. J.*, 1, 49.

Hill, L. (1941) *The Times*, July 17.

Klieger, I. S. (1940) *Clin. Med. Surg.*, 47, 242.

FOOD POISONING

See also B.E.M.P., Vol. V, p. 401.

Clinical Picture*Hyperemesis hiemis (winter-vomiting)*

Spore-forming bacteria in milk.—J. Zahorsky regards hyperemesis hiemis, or winter-vomiting disease, as a distinct clinical entity. It begins abruptly, with vomiting as the first symptom, and sometimes with symptoms of collapse. The vomiting continues for 1 or more days, everything swallowed being promptly ejected. An important diagnostic symptom is looseness of the bowels which begins a few hours after the vomiting. It is characterized by the passage of light-coloured stools with an offensive odour. Colicky pain may be considerable. The temperature in uncomplicated cases is not high (99° to 101° F.). The pulse is rapid and respiration is increased. There is evidence that the condition may be due to the presence of spore-forming bacteria in milk.

Zahorsky, J. (1940) *Arch. Pediat.*, 57, 666.

FOOT, DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. V, p. 412; and Surveys and Abstracts 1939, p. 342; 1940, p. 302.

Deformities*Congenital deformities*

Supernumerary metatarsal bone.—T. Horwitz reports a case of a girl of 16 with a supernumerary metatarsal bone and toe. The left foot was considerably broader than the normal right foot, and presented six well-developed toes. X-rays revealed the presence of 6 metatarsal bones. The 6th bone was in the valgus position, and was foreshortened, its shaft bowing outwards, and its broad base being articulated with the cuboid bone and with the base of the 4th metatarsal bone. The 4th metatarsal was in slight varus position, and presented some maldevelopment of its head.

Acquired deformities

Foot disease and military service.—R. Scherb, M. R. Francillon, and E. Burckhardt describe their experiences in military hospitals and Army service regarding diseases of the feet. Symptoms and functional disturbance are often much more intense in patients with very few organic findings than vice versa. Various diseases and deformities of the feet are described. Pain without objective signs occurs among other symptoms when additional bones, such as os fibiale externum, are present. Local pain of the short foot muscles may be due to over-exertion. Chronic deforming adhesions may cause great diagnostic difficulties. The most important deformities are flat foot and hallux valgus. In very severe contracted flat foot, rest in bed for 2-3 weeks is necessary. It was found that the percentage of patients with foot diseases has increased with the general mobilization of the Swiss Army, probably due to the

call-up of older men. The diagnostic difficulties of the regimental surgeons are alleviated by regular orthopaedic examinations of suspected cases in the brigade hospital. The orthopaedic unit decides whether or not the patient should stay with his unit or go to hospital. Even if an arch support only is fitted it is advisable to keep the patient in hospital under observation for a few days. Afterwards, patients go to a convalescent section where three companies are formed: (1) Convalescents under regular treatment or control, who march without kit and weapons; (2) convalescents under medical control: they march with weapons but without kit, and do guard duty; (3) convalescents who have recovered; these undertake full duties in a training company, for later transfer to active service. The men in the convalescent section are treated and controlled by orthopaedic surgeons. Arch supports should be individually constructed and technical details are given. The support should really 'support' the foot and must not move in the shoe or boot; metal supports are best, and the arch of the support should begin under the body of the os calcis.

Horwitz, T. (1940) *Amer. J. Surg.*, **50**, 578.

Scherb, R., Francillon, M. R., and Burckhardt, E. (1940) *Schweiz. med. Wschr.*, **70**, 701.

FUNGUS DISEASES

See also B.E.M.P., Vol. V, p. 448; Cumulative Supplement, Key Nos. 529-544; and Surveys and Abstracts 1939, pp. 64 and 342; 1940, p. 304.

Ringworm Infections

Ringworm of the feet and hands

Preventive treatment.—F. Reiss, discussing the prevention of dermatophytosis of the hands and feet, recommends the use of sodium thiosulphate solutions as foot-baths in all swimming-pools, to be used before and after bathing. An effective strength is one per cent, and fresh solutions should be provided every 24 hours.

Rarer Infections

Chromoblastomycosis

On wrist.—C. W. Emmons, Howard Hailey, and Hugh Hailey report a case of the rare fungus disease, chromoblastomycosis, in a man aged 68. In this case the aetiological agent was *Hormodendrum pedrosoi*. The lesion, which was of 3 months' duration, was on the dorsal aspect of the left wrist, and was 4 centimetres in diameter, elevated, bluish-red, boggy to the touch, and had multiple points of discharge. The case responded well to potassium iodide therapy.

Dermatophytides

Treatment

Dermatophytosis pedis.—M. Seldowitz describes a new and simple method of treating dermatophytosis pedis. This consists of the patient wearing ordinary leather insoles; the air in the pores of the leather is evacuated and replaced by rubber; it is impregnated with 8-hydroxy-quinoline, parachlorometaxyleneol, and chlorothymol. Of 40 patients with positive cultures and mycelia demonstrated on direct microscopical examination, 29 (72.5 per cent) were cured, clinically and mycologically, in an average of 4 months. Of 19 patients with negative cultures but with mycelia demonstrable on direct microscopical examination, 15 (80 per cent) were cured in an average of 2½ months. Of 51 with negative cultures and no microscopic findings, 51 (100 per cent) were cured in an average of 2 months.

Emmons, C. W., Hailey, Howard, and Hailey, Hugh (1941) *J. Amer. med. Ass.*, **116**, 25.

Reiss, F. (1941) *Urol. cutan. Rev.*, **45**, 328.

Seldowitz, M. (1940) *Arch. Derm. Syph., N.Y.*, **42**, 576.

GALL-BLADDER AND BILE-DUCTS

See also B.E.M.P., Vol. V, p. 477; Cumulative Supplement, Key Nos. 545-550; Surveys and Abstracts 1939, pp. 48 and 344; 1940, pp. 13 and 305.

Physiology

Disturbance of function

X-ray appearance in biliary dyskinesia.—B. Copleman and M. L. Sussman report 4 cases in which, after cholecystography and the ingestion of a suitable meal, the cystic, common, and hepatic ducts were outlined. This finding was considered unusual and presumably due to a disturbance in the reciprocal relationship of gall-bladder contraction and relaxation of the sphincter of Oddi. The clinical symptoms in these cases were similar to those described as forming the syndrome of biliary dyskinesia.

Gall-Stones

Cholesterosis of gall-bladder (strawberry gall-bladder)

Aetiology.—W. A. Mackey reports a case of cholesterosis of the gall-bladder in a woman aged 53. Histological examination of material obtained at operation indicated that lipid material in solution was in process of resorption from the bile, that it was gradually concentrated in globules, and that it was finally carried off by the lymphatics. In some conditions, e.g. when the bile is unusually rich in fat, the lipid in transit through the wall of the gall-bladder becomes visible to the naked eye. It is reasonable to suppose that, when polyps are

present, the lymphatics of the tumour pedicle have difficulty in handling the lipid absorbed by the great area of the mucosa of the polyp, and that as a result excessive stromal deposit occurs.

Cholecystitis

Cholecystography

Visualization of the gall-bladder by gas.—P. Kerley records the case of a woman, aged 52, who 2 weeks after the onset of an attack of severe pain in the gall-bladder, was tested by oral cholecystography; absorption of the dye was not seen, but the gall-bladder distended with gas was clearly visible. At operation the fundus of the gall-bladder, which was full of faceted calculi some half an inch wide, was densely adherent to the proximal third of the transverse colon; dissection showed that these adhesions enclosed a fistulous passage of some standing between the viscera, admitting the little finger. The gall-bladder was removed and the fistula closed. This visualization of the gall-bladder by gas does not appear to have been previously recorded. Two other possible methods by which the gall-bladder might be filled with gas are suggested: (a) infection by gas-forming organisms, and (b) the passage through the bile-ducts of a stone into the duodenum with consequent temporary atony of the ducts allowing air to pass up from the duodenum. This biliary dyskinesia is well known and there are many records of bismuth or barium ascending the bile-ducts.

Diseases of Bile-Ducts

Carcinoma of bile-ducts

Extra-hepatic.—M. M. Leiber, D. R. Morgan, and H. L. Stewart report 6 new cases of primary carcinoma of the extra-hepatic bile-ducts, one found in a series of 3,528 necropsies, and 5 in a series of 22,152 necropsies. The average age was 59·3 years; in 3 cases persons aged 29, 31, and 32 were affected. Of 98 reported cases 73 were in men.

Non-traumatic rupture of the common bile-duct

H. N. Taube and H. A. Himel under the above heading describe a rarely recognized condition, of which reference is made to 5 reported cases. The patient, a woman aged 30, gave a strong family history of gall-bladder disease; her mother was the subject of a cholecysto-gastric fistula, and her brother, aged 19, underwent cholecystectomy for cholecystitis and gall-stones. For 3 years she had had mild attacks of gall-bladder pain, and then came a severe bout of such intensity that 3 injections of morphine and atropine were given within an hour with very little benefit. This attack was followed by fever, a progressive leucocytosis (18,000–25,000), pulse 120, and an unusual amount of tenderness in the posterior lumbar region and the right lower quadrant. Laparotomy showed much free bile in the peritoneal cavity which presented little reaction, areas of fat necrosis in the great omentum, a thickened and distended, but not acutely inflamed gall-bladder containing faceted calculi, and where the common bile-duct passed under the duodenum there was an oedematous, dark brown cystic mass with leakage of bile; apparently rupture of the common bile-duct had taken place here, and become partially sealed off. For 7 days improvement followed, but then signs of local suppuration became obvious, and 29 days after the first operation a further exploration made it clear that there was a retroperitoneal abscess about the head of the pancreas. This was drained and the patient recovered.

Copleman, B., and Sussman, M. L. (1941) *Radiology*, **36**, 465.

Kerley, P. (1940) *Brit. J. Radiol.*, **13**, 289.

Leiber, M. M., Morgan, D. R., and Stewart, H. L. (1940) *Arch. Surg., Chicago*, **41**, 662.

Mackey, W. A. (1941) *Brit. J. Surg.*, **28**, 462.

Taube, H. N., and Himel, H. A. (1941) *Canad. med. Ass. J.*, **44**, 607.

GASTRITIS

See also B.E.M.P., Vol. V, p. 533; Surveys and Abstracts 1939, p. 47; 1940, p. 311; and p. 3 of this volume.

Aetiology

Syphilis

Signs and symptoms.—According to W. G. Morgan, there is not at present any recognizable diagnostic symptom-complex or pathognomonic sign of gastric syphilis. The following points were common to most of the author's series of cases: the peptic power of the stomach was low. The benzidine reaction for occult blood was positive at one time or another. There was gastric pain uninfluenced by the character of food, and this pain became worse towards night. There was stagnation of the gastro-intestinal contents, food remaining for hours in the stomach, although there was not any actual organic stenosis of the pylorus, as the results of the duodenal bucket-test showed. The stomach was considerably dilated and atonic. The duration was somewhat longer and the degree of physical deterioration was not so severe as in carcinoma of the stomach for the same length of time. In most cases the blood showed increased lymphocyte and eosinophil counts, with a moderate degree of chloro-anaemia. Notwithstanding the low peptic power, the appetite was keen and the food was relished. Vomiting occurred at some time during the course of the illness. There was nothing significant about the faeces. On examination of the abdomen the recti showed constant tendency to pass into

spasm when palpated. For this reason a tumour mass might not be so easily recognized as it would be in carcinoma of the stomach.

Morgan, W. G. (1940) *Urol. cutan. Rev.*, **44**, 479.

GLANDULAR FEVER

See also B.E.M.P., Vol. V, p. 559; and Surveys and Abstracts 1939, p. 348; 1940, p. 312.

Aetiology

Agglutination tests

Listerella group.—C. A. Janeway and G. J. Dammin tested the sera of 5 normal adults, 15 patients with miscellaneous diseases, and 13 patients with infectious mononucleosis for agglutinins against sheep cells and a representative strain of each of two known serological groups of the genus *Listerella* (*Bact. monocytogenes*). The results of the sheep-cell agglutination tests were in accordance with the findings of many previous workers. The results of the *Listerella* agglutination tests showed a slightly elevated titre in the sera of the patients with infective mononucleosis as compared with the control sera. The authors conclude that there is no definite aetiological relation between the known *Listerella* organisms and infectious mononucleosis.

Clinical Picture, Course, and Prognosis

Complications

Splenic rupture.—R. B. King records the very rare event of rupture of the spleen in glandular fever (infectious mononucleosis) in a man aged 23. Only one case (W. Attlee 1932) has been previously reported, accompanying Vincent's angina, but it was probably an unrecognized case of infectious mononucleosis. Intense abdominal pain, seemingly not preceded by any straining or spleen enlargement, was the first indication of the lesion in the case under review. Blood-streaked mucus was vomited and the abdomen became tense and right. Blood examination showed an increase in atypical lymphocytes and a decrease in neutrophils. There was no anaemia and no reduction in the number of platelets. The sheep-cell agglutination test for infectious mononucleosis was positive. Throat smears showed organisms typical of Vincent's angina. At operation, the spleen was enlarged and ruptured and draining blood freely and the histological structure was compatible with infectious mononucleosis. The appendix as well as the spleen was removed but its condition was not characteristic of infectious mononucleosis. No previous history of chronic splenomegaly is mentioned in the report.

Variations in clinical types

Simulating diphtheria.—K. C. Ch'en and C. T. Teng report a case of sporadic glandular fever (infectious mononucleosis) in a Chinese infant aged 11 months; the disease was at first regarded as diphtheria. The unusual clinical manifestation of laryngeal obstruction was present. The clinical features, characteristic blood findings, and positive serological tests established the diagnosis beyond doubt.

Blood picture

Atypical form.—G. Reyersbach and T. F. Lenert report on 16 cases of an atypical form of infectious mononucleosis in children. None of the children had symptoms or signs of any sort. The diagnosis was made entirely on the blood picture, which showed a higher leucocyte count, with a striking increase in apparently normal lymphocytes. The Paul-Bunnell test was uniformly negative. There was no evidence that the disease was due to infection with organisms of the *L. monocytogenes* group.

Differential Diagnosis

Angina of the throat

Associated with mononucleosis.—C. J. Fuller reports 5 cases of angina of the throat associated with mononucleosis and resembling the anginose type of glandular fever. In 2 of these cases the Paul-Bunnell test was negative, in 2 it was below the diagnostic level of titre, and in the fifth it was not performed. The author considers that either the Paul-Bunnell test is not always positive in glandular fever, or the condition described is due to some factor not yet explained. It is characterized by mononucleosis, a generalized lymphoid hyperplasia, and angina of the throat, and it responds well to treatment of the predominating organism found in the throat.

Attlee, W. (1932) *Lancet*, **1**, 291.

Ch'en, K. C., and Teng, C. T. (1941) *Chin. med. J.*, **59**, 116.

Fuller, C. J. (1941) *Lancet*, **1**, 69.

Janeway, C. A., and Dammin, G. J. (1941) *J. clin. Invest.*, **20**, 233.

King, R. B. (1941) *New Engl. J. Med.*, **224**, 1058.

Reyersbach, G., and Lenert, T. F. (1941) *Amer. J. Dis. Child.*, **61**, 237.

GOITRE AND OTHER DISEASES OF THE THYROID GLAND

See also B.E.M.P., Vol. V, p. 599; Cumulative Supplement, Key Nos. 569–574; and Surveys and Abstracts 1939, p. 352; 1940, p. 314.

Simple Goitre

Aetiology

Geological distribution of fluorine.—D. C. Wilson considers that the distribution of endemic goitre in the Punjab and in England is related to the geological distribution of fluorine

and to the distribution of human dental fluorosis (mottled enamel). Investigation showed the presence of dental fluorosis among school children in two areas in Somerset where two previous observers had recorded a high incidence of goitre, and the absence of dental fluorosis in an adjoining area where endemic goitre was absent.

Toxic Goitre

Pathology

Calcium and phosphorus metabolism.—G. E. Beaumont, E. C. Dodds, and J. D. Robertson report observations on calcium and phosphorus metabolism in 33 thyrotoxic patients (males 5, females 28) and 9 healthy controls (males 3, females 6). A review of the clinical, biochemical, radiological, and post-mortem appearances of the skeleton leaves no doubt that in toxic goitre a continuous decalcification is in progress. The following hypotheses have been suggested to explain the mechanism of this change: (1) increased basal metabolism *per se*, (2) increased excretion of phosphorus, (3) vitamin D deficiency, (4) direct stimulating catabolic effect of thyroxine on bone, and (5) coexisting hyperparathyroidism. Of these various causes for the increased mobilization and excretion of calcium in thyrotoxicosis, chief interest has centred around the last two; in order to determine, if possible, whether the calcium excretion depends on the direct action of thyroxine on bone or on an associated hyperparathyroidism, this chemical research, involving analyses of food, faeces, and urine, was undertaken. The calcium and phosphorus balances in normal men and women on a low intake of these minerals (calcium 100–150 milligrams daily; phosphorus 350–450 milligrams daily) showed a constant negative balance for both. The calcium and phosphorus metabolism of the 33 thyrotoxic patients also showed a constant negative balance for the two minerals, but the average loss was greater than in the normal subjects. On iodine medication a symptomatic improvement occurred in all cases, the basal metabolism fell, and the mean calcium and phosphorus excretion also diminished. After subtotal thyroidectomy a further fall in the basal metabolism invariably occurred and this was accompanied by a further diminution in the mean calcium and phosphorus excretion. This evidence would appear to favour the view that the increased loss of calcium and phosphorus in thyrotoxicosis is due to the direct effect of thyroxine on bone. Further analysis, however, shows that this is not a satisfactory explanation: thus (1) in almost half the cases (15 out of 33) the excretion of both calcium and phosphorus was within the limits of the normal controls; (2) there was not any correlation between the severity of the thyrotoxicosis and the calcium and phosphorus loss, e.g. the most severe case of thyrotoxicosis showed a normal mineral metabolism; (3) although iodine caused a remission in all cases with a fall in the level of the basal metabolism, in only 55 per cent of the cases did the calcium and phosphorus excretion diminish; (4) in 6 cases the calcium excretion remained the same after a successful thyroidectomy as before. These considerations suggest that some cause other than the direct action of thyroxine on bone must be sought to account for the decalcification and excessive loss from the body of calcium and phosphorus in thyrotoxicosis.

Clinical picture

Excretion of hippuric acid in hyperthyroidism.—S. F. Haines, T. B. Magath, and M. H. Power state that the excretion of hippuric acid in Quick's test is reduced in a considerable number of cases of hyperthyroidism. This conforms to the opinion widely held that the liver is often functionally disturbed in this disease. The reduction in excretion of hippuric acid is correlated inversely to a slight degree with the basal metabolic rate. Excretion of hippuric acid is generally diminished when the bromsulphthalein test shows retention of dye, and is also decreased in some other cases.

Treatment

Ergot alkaloids, ergotoxine and ergotamine.—D. E. Brace and L. C. Reid state that the ergot alkaloids, ergotoxine and ergotamine, are useful adjuncts to the surgical management of thyrotoxicosis. Two periods when tachycardia becomes a serious and alarming manifestation are during and for 24 to 72 hours after operation. In such cases the pulse rate appeared to be better controlled by ergotoxine-ergotamine therapy than in a control series without that treatment. These drugs do not exert any recognizable effect on the tachycardia of anoxia.

Tumours

Malignant

Thyroid carcinoma.—D. N. Matthews reports a case of malignant adenoma of the thyroid in a woman, aged 20 years, who had had an enlarged thyroid for 15 years. Two sections were examined microscopically: one showed a foetal adenoma, the other a malignant adenoma with a papilliferous structure in some parts.

Beaumont, G. E., Dodds, E. C., and Robertson, J. D. (1940) *J. Endocrinol.*, **2**, 237.

Brace, D. E., and Reid, L. C. (1941) *Ann. Surg.*, **113**, 62.

Haines, S. F., Magath, T. B., and Power, M. H. (1941) *Ann. intern. Med.*, **14**, 1225.

Matthews, D. N. (1941) *Proc. R. Soc. Med.*, **34**, 325.

Wilson, D. C. (1941) *Lancet*, **1**, 211.

GONORRHOEA

See also B.E.M.P., Vol. VI, p. 1; Cumulative Supplement, Key Nos. 575-578; Surveys and Abstracts 1939, pp. 155 and 356; 1940, pp. 90 and 318; and p. 107 of this volume.

Bacteriology*Specific hypersensitivity*

Diagnostic cutaneous test.—B. C. Corbus and B. C. Corbus, Jun. believe that a person infected with a specific organism is in a state of hypersensitivity to that organism as long as it remains within the body. They have found the following cutaneous test to be a valuable adjunct in the diagnosis of gonococcal infections. A 25 to 27 gauge needle, attached to a standard tuberculin syringe, is introduced into the skin of the extensor surface of the upper arm, parallel to the surface of the skin, and advanced slowly with the bevel upwards, penetrating the papillary layer to a depth of somewhat less than a millimetre. There is then injected 0.1 cubic centimetre of a standard filtrate of gonococcus and 0.1 cubic centimetre of a broth control. When the injection has been correctly performed, in positive cases a wheal appears which is not translucent, but white and sharply circumscribed, with a rose-pink border.

Pathology*Gonococcal septicaemia*

Association with endocarditis.—J. S. Davis, Jun. records 14 examples of gonococcal septicaemia. In 12 of these the diagnosis was confirmed by necropsy; as one recovery occurred in the remaining 2 patients the presence of gonococcal endocarditis was not certain, nor were gonococci obtained by blood culture. A review of previous work on gonococcal septicaemia and endocarditis is given, and it is probable that they are commoner than is generally recognized, and that a diagnosis may be long delayed; the diagnosis may be difficult, for the blood cultures may be negative, petechiae are rare, and a case is reported in which the acute septicaemic attack, at first regarded as rheumatic fever, occurred 40 years after the original gonorrhoea. The patients seemed to be prone to pneumonia. The most distinctive cutaneous lesions that may occur in gonococcal bacteraemia are given: (1) keratoderma blenorrhagicum and variants, but the author cannot quote any recorded case associated with gonococcal endocarditis; (2) a haemorrhagic vesiculo-pustular and bullous lesion, somewhat like the previous form, but giving a positive culture more readily; there is not any record of association with gonococcal endocarditis; (3) lesions resembling Osler's nodes—these are rare; (4) purpura; and (5) petechiae, which may occur in the absence of gonococcal endocarditis.

Gonorrhoea in Males*Treatment*

Albucid.—R. Marinkovitch investigated the use of albucid in 100 male patients with gonorrhoea. The author claims that albucid is better tolerated than other sulphonamides, and that nausea and vomiting are completely absent after its use. He obtained a cure rate of 91 per cent. The results were slightly better than those obtained in a parallel series of cases treated with sulphapyridine. The dosage was 1.5 grammes by mouth, 3 times a day for 6 days, and 1 gramme 3 times a day on the seventh day.

Sulphapyridine.—C. Ferguson, M. Buckholtz and R. A. Hingson have tested the use of sulphapyridine in gonococcal infections which have previously resisted sulphanilamide. Gonococcal infections fail to respond to sulphanilamide in some patients even though given in adequate doses; moreover, the treatment is sometimes inadequate when it is given to out-patients and self-medication is attempted. Such inadequate dosage appears to raise the resistance of the infection to the drug. The authors treated 100 men between the ages of 20 and 40 with sulphapyridine; they were all seafaring men in good health and all had previously been adequately treated with sulphanilamide. The dosage was 1 gramme of sulphapyridine every 4 hours day and night for 2 days, then 0.5 gramme every 4 hours day and night for 4 to 8 days. The fluid intake was limited to 1 quart per 24 hours, or 1½ quarts during the summer months. Cure was obtained in 75 per cent of the cases, the criteria of cure being disappearance of urethral discharge and urine clear by the two-glass test, and urethro-prostatic secretion negative for gonococci by smear and culture. Three such reports at 2-day intervals were required. The authors are now using sulphapyridine for routine hospital treatment of gonococcal infections. They have not seen any serious side effects, but emphasize the need for daily clinical observation while the drug is being given.

Sulphathiazole.—L. Stockwell reports on the use of sulphathiazole on 30 ambulatory and 3 hospital cases of gonorrhoea in the male. A permanent cure resulted in all cases. The drug proved effective in all stages of the disease, and in patients resistant to previous sulphonamide therapy. Epididymitis responded well to the drug. With regard to dosage, the best results were obtained by giving 10 grammes during the first 24 hours (in divided doses of 2 grammes every 4 hours for 5 doses); during each of the next 24-hour periods 5 grammes were given until a total of 20 grammes, when the drug was discontinued. With this dosage in all cases discharge ceased and a negative smear and culture were obtained within 1 to 2 days.

J. G. Strohm, W. E. Nielsen, and P. B. Potampa report on the use of sulphathiazole in the treatment of gonorrhoea in 31 males. An analysis of 100 cases of sulphanilamide treatment with local therapy indicates only 20-30 per cent efficacy for that drug. Sulphathiazole with local therapy cured the 31 patients without any recurrence or reactions. The treatment is as follows: if the second glass is clear in the two-glass test for urethritis, the anterior urethra

is irrigated with warm acriflavine solution (1:4,000 dilution). Afterwards one gramme (15 grains) of sulphathiazole is given every 6 hours for the first 2 days; half a gramme ($7\frac{1}{2}$ grains) every 4 hours for 2 days, descending to 6-hourly doses. After 5 or 6 irrigations twice weekly, potassium permanganate is substituted for acriflavine. The test for cure is begun when both glasses are clear and free from infected shreds. If the urine remains clear after three silver nitrate irrigations, the prostate is massaged and the fluid examined for pus cells. If they are present the prostate is massaged and irrigated twice weekly. The sound is then used and if there is no reaction in 1-4 days the patient is discharged as cured.

F. Knight, C. A. W. Uhle, and L. W. LaTowsky treated 55 male patients with gonococcal urethritis with sulphathiazole. Of 50 patients, 96 per cent were cured after an average of 8 days' treatment with an average of 28 grammes of the drug. Toxic reactions occurred in only 11.5 per cent of cases. The average time for a bacteriological cure was 28 days.

Sulphathiazole and sulphapyridine.—D. K. Hibbs, A. A. Day, Ruth W. Jung, and J. M. Brady report on the use of sulphathiazole and sulphapyridine in gonorrhoea in the male. Both drugs are effective. The clinical symptoms subside earlier under sulphapyridine treatment than under sulphathiazole. The percentage of failures is higher among those on sulphapyridine (17.5 per cent) than in those on sulphathiazole (5.26 per cent). Sulphathiazole appears to be less toxic than sulphapyridine.

Sulphathiazole and sulphamethylthiazole.—T. M. Burkholder and F. Bang treated 125 patients with acute and chronic gonorrhoeal urethritis with sulphamethylthiazole and sulphathiazole. All the patients, except 8, were apparently cured. The latter, although clinically improved, had positive cultures after 14 days' treatment. The dosage recommended is 4 to 5 grammes initially, followed by 1 gramme every 4 hours for 14 days. The average blood concentration of sulphathiazole was 6 milligrams per cent. The authors preferred sulphathiazole because it produced a high percentage of cures and few subjective reactions.

Toxic effects of sulphathiazole.—E. A. Glicklich and D. S. Sherman describe toxic manifestations similar to those of acute gonococcal arthritis, resulting from the administration of sulphathiazole to a patient with symptoms of chancroidal infection and gonorrheal urethritis of 10 weeks' duration. The blood contained 72 per cent haemoglobin, 9,800 leucocytes per cubic millimetre, and the urine was normal except for the presence of 10-15 leucocytes in the high-power field. Sulphathiazole (6 grammes daily) was given by mouth 1 day after admission, and after 3 days the patient's temperature rose to 100° F. Malaise, prostration, nausea, headache, burning and itching of the eyes, and maculopapular eruptions of the extremities occurred on the fifth day. These symptoms were accentuated on the sixth and seventh days and a rash, like that of erythema nodosum, appeared on the extremities. The scleras and conjunctivas became injected. The haemoglobin count was 100 per cent, the leucocyte count 24,000 per cubic centimetre, and the total sulphathiazole level in the blood was 8.6 milligrams per 100 cubic centimetres. The urine was normal. Fluid drawn from a swelling on the knee was sterile and contained sulphathiazole, showing that the swelling was a toxic manifestation of the drug. The symptoms subsided on suspension of the drug for a week and on readministration recurred with the addition of abdominal cramps. The blood contained 84 per cent of haemoglobin, 11,700 leucocytes per cubic millimetre, and a total of 3.9 milligrammes of sulphathiazole per cubic millimetre. The urine was normal. The patient recovered satisfactorily from the toxic effects and from the gonorrheal infection.

Gonorrhoea in Both Sexes

Treatment

Artificial fever and chemotherapy.—H. W. Kendell, D. L. Rose, and W. M. Simpson treated 83 patients with complications of gonorrhoea resistant or intolerant to chemotherapy, with artificial fever either alone or combined with chemotherapy. Of 25 patients receiving fever therapy alone, only 12.5 per cent were cured after a single 8-hour treatment at 106.6° F., and 62.5 per cent were cured after a single 10-hour treatment at 106.6° F. All of 31 patients treated with chemotherapy for 18 hours before a single 10-hour fever session at 106.6° F. were cured.

Gonococcal septicaemia.—The forms of treatment for gonococcal septicaemia, suggested by J. S. Davis, Jun. are (1) sulphanilamide up to 150 grains (9.7 grammes) which must be carefully watched, as in a recent case of subacute bacterial endocarditis a dosage of 80 to 200 grains daily for 3 weeks caused the leucocyte count to fall from 25,500 to 200; (2) artificial fever induced by the Kettering hypertherm; (3) blanketing the patient, thus utilizing the patient's body heat to maintain a fever; (4) multiple blood transfusions; and (5) surgical removal of any focus of infection.

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Corbus, B. C., and Corbus, Jun., B. C. (1941) *J. Amer. med. Ass.*, **116**, 113.

Davis, J. S., Jun. (1940) *Arch. intern. Med.*, **66**, 418.

Ferguson, C., Buckholtz, M., and Hingson, R. A. (1940) *Amer. J. med. Sci.*, **200**, 365.

Glicklich, E. A., and Sherman, D. S. (1941) *Arch. Derm. Syph., N.Y.*, **43**, 992.

Hibbs, D. K., Day, A. A., Jung, Ruth W., and Brady, J. M. (1941) *J. Urol.*, **45**, 727.

Kendell, H. W., Rose, D. L., and Simpson, W. M. (1941) *Arch. phys. Ther.*, **22**, 103.

- Knight, F., Uhle, C. A. W., and LaTowsky, L. W. (1940) *J. Urol.*, **44**, 748.
 Marinkovitch, R. (1941) *Lancet*, **1**, 144.
 Stockwell, L. (1941) *J. Urol.*, **45**, 636.
 Strohm, J. G., Nielsen, W. E., and Potampa, P. B. (1941) *Northw. Med.*,
Seattle, **40**, 202.

GOUT

See also B.E.M.P., Vol. VI, p. 37; Cumulative Supplement, Key No. 579; and Surveys and Abstracts 1939, p. 359; 1940, p. 321.

Diagnosis and Differential Diagnosis

Twenty-one diagnostic features

Contrary to general belief, P. S. Hench holds that gout is fairly common, although often unrecognized, in America. Most patients with gouty arthritis endure a number of attacks before a correct diagnosis is made; this is unfortunate, because of all the various articular diseases, acute gouty arthritis is one of the most responsive to treatment, especially by a few doses of colchicine ($\frac{1}{100}$ grain) every 2 or 3 hours, a brisk cathartic of magnesium sulphate ($\frac{1}{2}$ to 1 oz.), and rest, preferably in bed. The diagnosis is therefore of most obvious importance. Hench's 21 diagnostic features of gout and gouty arthritis are mentioned in order below. (1) Acute arthritis after trivial injuries. (2) Onset after dietary excess of holidays, birthdays, and the like. (3) Onset within a week after a surgical operation. (4) After trauma, exposure, and dietary excesses (venison, meat, alcohol) of a fishing or hunting trip. (5) Recurring acute attacks in the spring or autumn. (6) Onset between 2 and 7 a.m. (7) Onset while the patient is taking liver extract for anaemia, salyrgan for dropsy, ergotamine tartrate for migraine, a ketogenic diet, thiamine hydrochloride (vitamin B₁), dehydrocholic acid (decholin), or insulin (rarely); these are medicinal provocatives of gout. (8) Acute arthritis in leukaemia, polycythaemia, or other dyscrasias involving haemolysis and liberation of nucleoproteins are also indicative of gout. (9) Be cautious in diagnosing gout in females, as 98 per cent of cases are in males. (10) Suspect as gouty any acute arthritis which suddenly and spontaneously occurs in a man over 40 years of age, such cases are most often gout. (11) Suspect acute arthritis suddenly producing maximal disability with dramatic speed in a few minutes or hours. (12) Suspect gout when the pain of an acute, but short-lived, arthritis is usually severe; (13) with acute inflammation of the great toe, especially when the maximal tenderness is on its mesial aspect; (14) when an acutely affected foot is warm and red or bluish red rather than cold and bluish white as in rheumatoid arthritis, and when oedema and later desquamation of the skin follow; (15) when the patient wears a split shoe or a cut-out shoe; (16) when there is acute arthritis of short duration which from its severity disappears rather rapidly and completely; (17) if a patient with chronic arthritis has previously had recurrent acute attacks with complete remissions. (18) Since olecranon bursitis is several times commoner in gout than in any other disease, its presence should suggest consideration of gout. (19) When the shoulders, hips, or spine are acutely or chronically affected a diagnosis of gout should only be made on indisputable evidence. (20) In acute or chronic arthritis with a history of renal calculi gout should be thought of, and also (21) in the presence of peri-articular or para-articular ulcers or fistulas. Ulcerating gouty tophi are now more common than ulcerating tuberculous fistulas of joints. The toxicity of cinchophen is carefully considered; in acute gout a dose of cinchophen, $7\frac{1}{2}$ grains, 3 or 4 times a day is recommended with precautions, such as 2 litres of fluid daily, alkalis and carbohydrates. Serious reactions, however, are stated to be rare, especially in gout; the risk of fatality is believed to be only a small fraction of 1 per cent.

Hench, P. S. (1941) *J. Amer. med. Ass.*, **116**, 453.

GRANULOMA, ULCERATIVE

See also B.E.M.P., Vol. VI, p. 54; Cumulative Supplement, Key No. 580; and Surveys and Abstracts 1940, pp. 91 and 322.

Treatment

Sulphapyridine

With foudadin (stibophen).—K. V. Earle employed sulphapyridine in 6 cases of ulcerative granuloma; various combinations of antimony salts were also given. Favourable results were obtained by combinations of injections of foudadin (stibophen) with sulphapyridine orally. A case of mixed infection (ulcerative granuloma and lymphopathia venereum) also responded to this therapy. This treatment is suggested as deserving further trial.

Earle, K. V. (1940) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 261.

HAEMATOPORPHYRINURIA

See also B.E.M.P., Vol. VI, p. 85; and Surveys and Abstracts 1939, p. 361; 1940, p. 323.

Clinical

Haematoporphyrinuria acuta

Complicated by acute polyneuritis.—L. Rau reports a case of acute idiopathic haematoporphyrinuria complicated by acute polyneuritis, in a woman aged 30 years in whom there was not any evidence that it was caused by any drug or toxin, nor could it be ascribed to allergy, rheumatism, or diet. Features of the case were that the attack was associated with the onset of the menstrual cycle, there was obstinate constipation and backache; acute peripheral

polyneuritis was observed on the fourth day. The patient was treated with injections of liver extract, insulin, glucose, and alkalis, and the polyneuritis cleared up.

Rau, L. (1940) *Lancet*, **2**, 647.

HAEMATURIA

See also B.E.M.P., Vol. VI, p. 97; and Surveys and Abstracts 1939, p. 361; 1940, p. 324.

Haematuria

Aetiology

Sulphathiazole.—J. H. Arnett reports haematuria in a woman, aged 72, who had received 14 grammes of sulphathiazole within 48 hours for pneumonia. The urine became loaded with blood, and the patient complained of intense pain in the lumbar region. The urinary output, which had been 960 cubic centimetres on the previous day, was 570 cubic centimetres plus an unknown quantity which was lost during defaecation. The sulphathiazole level in the blood was 7 milligrams per 100 cubic centimetres. The drug was stopped, and 900 cubic centimetres of 5 per cent dextrose in physiological saline solution were given intravenously. On the following day the pain had subsided, the haematuria was slightly less, although it was still full of blood cells and crystals, and the patient's condition improved. Convalescence continued slowly. Stress is laid on the importance of maintaining a sufficiently high fluid intake to prevent massive formation of crystals. The fluid intake and urinary output should be carefully watched, and the urine should be examined at least once a day for crystals and blood. If the intake can be kept in excess of 3,000 cubic centimetres, and the output at 1,500 cubic centimetres or more a day, and if the drug is immediately discontinued and intravenous fluids are administered with the first appearance of lumbar pain, or of haematuria, the dangers from renal complications are reduced to a minimum.

Arnett, J. H. (1940) *J. Amer. med. Ass.*, **115**, 362.

HAEMOCHROMATOSIS

See also B.E.M.P., Vol. VI, p. 106.

Clinical Picture

Anomalous symptoms

A. Cantarow and C. J. Bucher report a case in a coal miner, aged 45, of haemochromatosis without glycosuria, and of significant decrease in the dextrose tolerance in spite of the unusual quantity of iron in the liver and pancreas; the absence of iron-containing pigment in the apparently characteristic colour of the skin; the presence of cutaneous xanthomatosis and hypercholesterolaemia and hyperbilirubinaemia; the demonstration during life of deficiency of the adrenal cortical and androgen hormones; and the final cause of death, acute necrosis of the pancreas. For 4 years before death cutaneous pigmentation of the skin and intense itching had been present, for 3 years abdominal enlargement, and for 9 months oedema of the feet. Although the cutaneous pigmentation at once suggested haemochromatosis the above anomalies for a time threw doubt on this diagnosis, in favour of xanthomatous biliary cirrhosis (Thannhauser and Magendantz). Radiological examination showed moderate anthracosis of the lungs, diffuse demineralization of the entire skeleton, and enlargement of the liver and spleen. A large number of tests, including Cutler's for adrenal cortical function, were performed. The existence of haemochromatosis was established by examination of a piece of liver removed at peritoneoscopic examination; this showed a large liver, grey bronze in colour, with extensive multilobular cirrhosis, with much brownish iron-containing pigment (haemosiderin) with the characteristic distribution of haemochromatosis. This was confirmed at the necropsy, which showed that the spleen, like the liver, was enlarged, with chronic inflammation of the peritoneum and haemosiderin principally in the cells lining the sinusoids. The retroperitoneal lymphatic glands were heavily infiltrated with haemosiderin. The choroid plexus of the brain was also affected. The pancreas was dark brown where it was not necrotic or haemorrhagic; there was not any fat necrosis. The duodenum and first part of the jejunum were pigmented.

Cantarow, A., and Bucher, C. J. (1941) *Arch. intern. Med.*, **67**, 333.

Thannhauser, S. J., and Magendantz, H. (1938) *Ann. intern. Med.*, **11**, 1662.

HAEMOGLOBINURIA

See also B.E.M.P., Vol. VI, p. 115; and Cumulative Supplement, Key Nos. 588–593.

Clinical Picture

Haemoglobinuria due to chemical agents

Sulphanilamide.—D. R. Gilligan and I. Kapnick report a case, of a Negro aged 38, with haemoglobinuria occurring during an attack of acute haemolytic anaemia as a result of sulphanilamide therapy. The patient had received therapeutic doses of the drug. The haemolytic attack developed in the short period of 3½ days after the first dose of the drug. The red-cell count fell from 3,500,000 to 1,400,000 within 12 hours. At the height of the attack haemoglobinuria appeared and lasted 18 hours. Fever, leucocytosis, and jaundice occurred, but there were not any unpleasant symptoms. The patient was treated with blood transfusions, and made a good recovery.

Gilligan, D. R., and Kapnick, I. (1941) *New Engl. J. Med.*, **224**, 801.

HAEMORRHAGIC DISEASES

See also B.E.M.P., Vol. VI, p. 138; and Surveys and Abstracts 1939, p. 362; 1940, pp. 16, 31, and 325.

Primary Non-Hereditary Haemorrhagic Diathesis*Pathogenesis and morbid anatomy*

R. L. Haden and R. W. Schneider review 310 cases of the haemorrhagic diathesis and state that the two important factors in abnormal bleeding are the condition of the capillary endothelium and variations in the clotting mechanism. They consider that every patient with pathological haemorrhage should be examined to eliminate haemorrhagic disease. Platelet deficiency or lack of prothrombin is generally the cause of a defect in the coagulation mechanism. In laboratory work the most common abnormality in clinical cases is a prolonged coagulation time. Abnormal haemorrhage is more often due to an increased permeability of the vessel walls than to some defect in coagulation of the blood.

Thrombocytopenic purpura

Treatment with parathyroid.—D. B. Levine and H. Michelson successfully employed a solution of parathyroid in a case of thrombocytopenic purpura. Laboratory examination showed a red-cell count of 1,700,000, haemoglobin 25 per cent, platelets 25,000, white cells 16,400, polymorphonuclears 82 per cent, lymphocytes 16 per cent, monocytes 2 per cent, bleeding time more than 20 minutes, no clot retraction at the end of 24 hours, and tourniquet test highly positive in 1 minute. Blood transfusions, moccasin snake venom, and ascorbic acid having been employed without success, splenectomy was performed. Post-operative recovery was rapid, but the patient's condition then deteriorated and she appeared to be moribund. She was then given 50 units of a solution of parathyroid subcutaneously, which was increased to 100 units on the following day. A further 100 units was given next day, and 150 units on the day following. After this she improved rapidly and made an uneventful recovery. Eleven months later there had been no sign of relapse.

Aetiology, diagnosis, and treatment.—B. K. Wiseman, C. A. Doan, and S. J. Wilson consider that no single explanation for the production of essential thrombocytopenic purpura adequately accounts for all the known facts relating to the disease. That of splenic thrombocytolysis, however, seems to be most reasonable. In the differential diagnosis aspiration of bone marrow rules out leucopenic leukaemia, aplastic anaemia, pernicious anaemia, and neoplasia. History of drugs employed and contact with some infective diseases is also important. The only treatment effective in restoring platelet level in essential thrombocytopenia is splenectomy. Cases of symptomatic thrombocytopenia should not be submitted to operation.

Haemorrhagic Deficiency Disorders*Plasma-prothrombin titrations*

In infants.—G. Edsall made plasma-prothrombin titrations on 39 specimens of venous blood from 27 infants between the ages of 3 hours and 25 days. The titres ranged from 5 to 70+ per cent of the adult normal. Of 11 infants observed after neonatal asphyxia or intracranial haemorrhage, 9 had titres below 35 per cent. Although no absolute relation was observed between the prothrombin level and the tendency to haemorrhage, it was noted that infants with titres below 15 per cent were liable to severe bleeding; that those with intermediate levels (15 to 30 per cent) might, or might not, bleed; and that those with titres above 30 per cent sometimes had a transitory melaena; but did not show a severe bleeding tendency.

Treatment

Vitamin P.—I. N. Kugelmass employed a solution of vitamin P (a mixture of the glucosides hesperidin and eriodictyon) in several cases of vascular purpura. The vitamin material was prepared from orange peel according to the method of Szent-Györgyi (1938). The solution of 50 milligrams per cubic centimetre of flavines consisting of eriodictyol and hesperidin was given in doses of 150 milligrams orally. Successful results were obtained in the cases of 2 children with allergic purpura, a child with infective purpura, and an infant with nutritional purpura. The treatment was ineffective in 3 cases of mechanical purpura.

Hereditary Haemorrhagic Disorders*Familial purpura simplex*

Incidence of associated rheumatism.—E. Davis analysed the records of 27 families, comprising 88 members, with hereditary familial purpura simplex. Of these, 84 were females. Of the 88 patients, 78 had purpura simplex, 6 purpura of the Schönlein or Schönlein-Henoch type, 2 sustained bruises or trivial injuries, and 1, a boy, had pseudo-haemophilia. In 2 of the families familial telangiectasia occurred. Of the 88 subjects 23 had a history of rheumatic fever, 8 of rheumatoid arthritis, 15 of some other form of arthritis, and others of severe fibrositis. A special association between rheumatism and purpura is suggested.

Davis, E. (1941) *Lancet*, 1, 145.

Edsall, G. (1941) *New Engl. J. Med.*, 224, 762.

Haden, R. L., and Schneider, R. W. (1941) *Amer. J. clin. Path.*, 11, 263.

Levine, D. B., and Michelson, H. (1940) *J. Amer. med. Ass.*, 115, 360.

Szent-Györgyi, A. (1938) *Hoppe-Seyl. Z.*, 255, 126.

Wiseman, B. K., Doan, C. A., and Wilson, S. J. (1940) *J. Amer. med. Ass.*,

115, 8.

HAEMOTHORAX

See also B.E.M.P., Vol. VI, p. 156; Surveys and Abstracts 1940, p. 327; and p. 71 of this volume.

Treatment

Traumatic haemothorax

Clinical categories.—F. G. Chandler divides cases of traumatic haemothorax into three groups. (1) Simple and not infected cases may show small extravasations, with physical signs of fluid at the extreme base, and radiological evidence of fluid in the costophrenic sinus with the dome of the diaphragm visible. The administration of sulphonamide drugs to prevent infection is suggested. No active treatment is needed. If larger amounts of blood are present as shown by examination, treatment by aspiration and replacement of air or oxygen is indicated. The removal of any considerable amount of fluid without replacement of air or oxygen is dangerous as it may cause displacement of the mediastinum. (2) Infected cases, as shown bacteriologically, whether aerobic or anaerobic, or by an unpleasant odour in aspirated blood, whatever the bacteriological report, should be treated surgically. The question whether or not the presence of massive clotting of the blood—sometimes a difficult matter to decide—is evidence of infection, is raised. The treatment of infected cases is surgical. (3) Cases complicated by other factors, such as open wounds of the chest, foreign bodies, missiles, splinters of bone, clothing, damage to the lung, diaphragm, and other parts.

C. Hoyle also divides the cases into three categories. (1) The first includes simple, not infected cases. Treatment consists in blood rather than plasma transfusion for large haemorrhagic effusions, especially if the accumulation has taken place rapidly. Blood should be removed for bacteriological examination as regards infection. Apart from aspiration for mechanical reasons there are good grounds for routine air replacement; one of the most important is the length of time required for blood absorption, weeks or months, whereas aspiration followed by air replacement is effective in less than an hour; it also tends to prevent infection of the pleura. In a few cases of simple haemothorax massive clotting of blood occurs; failure to aspirate the haemothorax should arouse a suspicion of this event, but a dry tap may be due to the choice of too low a site, the diaphragm being usually at a high level. (2) The second group, of compound haemothorax, includes cases with evidence of serious damage to the chest wall and lung, and the presence of foreign bodies. Surgical treatment allows excision of the wounds, thorough evacuation of the pleural cavity, and the removal of damaged lung tissue and foreign bodies. (3) Infected haemothorax may arise several weeks after the injury. In the early stages the proper treatment is repeated aspiration as in an empyema; it is a mistake to insert a drainage tube until the infection has become localized.

G. A. Mason points out that injuries to the parietes, lung, mediastinum, heart, and abdominal viscera, when the diaphragm is torn, are among the causes of a traumatic haemothorax. Unless a large vessel is injured, bleeding in a closed haemothorax tends to cease spontaneously. In the absence of infection the haemothorax may be allowed to undergo absorption spontaneously, but usually aspiration and air replacement are desirable. Massive clotting may occur and either be absorbed or, becoming organized, cause gross distortion within the hemithorax, or eventually leave calcified masses. Continued or recurrent bleeding and the occurrence of infection are indications for exploratory operation.

Tudor Edwards deals with haemothorax from crushed chest now becoming more frequent owing to bomb casualties, and haemothorax due to missiles that have passed through the chest or associated with the retention of one or more small fragments or shells. When once the shock has passed off, the sooner the blood in the pleura is removed the better. There is not any risk of recurrent haemorrhage, if arising from the lung, provided that the blood removed is replaced by air in the same quantity. Early aspiration has the advantages that it removes the blood before it is clotted, it removes an excellent culture medium for bacteria, and because, if followed by air replacement, haemorrhage from damaged vessels in the chest wall can be diagnosed radiologically or by physical signs before the general manifestations of haemorrhage become obvious. If air replacement is not carried out, bleeding may continue without alteration in the physical or radiological signs, as the lung gradually collapses under the fluid. Further, aspiration prevents the late results of pleuritic fibrosis and chest contraction.

J. L. Livingstone, with an experience in Great Britain of 200 cases of chest wounds, refers to 115 cases of haemothorax, and advises aspiration and gas replacement in all but the slightest cases for the following reasons: (a) until the haemothorax has been removed and further radiograms taken it is impossible to be certain that the condition is not complicated; (b) prevention of infection; and (c) because removal of the blood shortens the period before recovery results. But if there is any doubt about the question of infection, air replacement should not be carried out. Infection may or may not occur in both 'simple' and 'compound' haemothorax, but cases with a retained foreign body in the chest are specially likely to become infected. Among the 115 cases 30 per cent were infected. In haemothorax a considerable exudation of fluid takes place during the first few days. The pleural cavity should be kept as dry as possible by aspiration.

Chandler, F. G. (1940) *Proc. R. Soc. Med.*, **34**, 73.

Edwards, A. T. (1940) *Proc. R. Soc. Med.*, **34**, 80.

- Hoyle, C. (1940) *Proc. R. Soc. Med.*, **34**, 75.
 Livingstone, J. L. (1940) *Proc. R. Soc. Med.*, **34**, 87.
 Mason, G. A. (1940) *Proc. R. Soc. Med.*, **34**, 78.

HAIR FOLLICLES, ABNORMALITIES AND DISEASES

See also B.E.M.P., Vol. VI, p. 162; and Surveys and Abstracts 1939, p. 363; 1940, p. 328.

Hirsuties

Hypertrichosis in the female

Adrenal hypertrophy.—R. Greene describes a case of hypertrichosis, in a woman aged 26, due to hypertrophy of the adrenal cortex. After a normal childhood and pubescence, she began at the age of 19 to show an excessive growth of hair. The whole body became more than normally hirsute, the eyebrows were thick, and the sides of the face, upper lip, and chin were covered with thick, black, coarse hair. The clinical diagnosis of adrenal hypertrophy was confirmed by an assay of male hormone excretion; whereas the normal range of excretion of 17-ketosteroids is 2.5 to 12.5 milligrams daily, the patient's values varied about an average of 19 milligrams, being always above the usual limits for a normal woman, and sometimes exceeded that figure. The patient did not excrete any sodium pregnandiol glycuronide, from which it may be assumed that progesterone was not excreted by her adrenal glands.

Pili Torti

G. E. Clarke and E. L. Glicksberg report a case of pili torti in a boy aged 14. The boy complained that his hair grew in all directions. Examination showed that his scalp was well covered with light hair growing as he described. The hair of the eyebrows, eye-lashes, and pubic region showed similar characteristics. Macroscopic and microscopic examination of individual hairs showed twisting through 180 degrees. The pathogenesis of pili torti is at present unknown.

- Clarke, G. E., and Glicksberg, E. L. (1941) *Arch. Derm. Syph., N.Y.*, **43**, 836.
 Greene, R. (1940) *Lancet*, **2**, 486.

HAND, DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. VI, p. 171; Cumulative Supplement, Key Nos. 613–617; and Surveys and Abstracts 1940, p. 329.

New Growths

Osteophytes

Heberden's nodes.—R. M. Stecher divides Heberden's nodes into two forms: (a) traumatic, due to an injury sufficiently severe to be remembered as regards time and circumstance, commoner in men and most often confined to one finger, or at least to one hand, and (b) idiopathic, without relation to injury, but a form of osteoarthritis, though rarely part of generalized osteoarthritis. Analysis of 68 families (white) with the incidence of the idiopathic form showed 66 females and 2 males; it is low until the age of 60 years and then rises rapidly to nearly 30 per cent in the ninth decade. It is regarded as familial and hereditary; of 67 mothers of affected women 21 were stated to have had Heberden's nodes; of 129 sisters of affected women 33 were said to have Heberden's nodes. In the control series, of 43 mothers of unaffected women, none were reported to show Heberden's nodes. Of 109 sisters of unaffected women, 5 were found to have the nodes.

Chronic Inflammatory and Miscellaneous Conditions

Ganglion

Injection treatment.—E. J. Ball reports good results from the injection treatment of ganglion by a proteolytic enzyme, caroid. This enzyme liquefies the gelatinous material, which can be freely aspirated. The solution employed is a suspension of the pulverized enzyme in sterile distilled water, 60 minims to each 5 cubic centimetres of water. One minim of hydrochloric acid is added to each 10 cubic centimetres of the suspension. The mixture is shaken vigorously and drawn into a 10 cubic centimetre syringe, with a 20 gauge needle. About 2 cubic centimetres is injected slowly into the ganglion. In 30 minutes liquefaction of the contents is complete. Twenty-four hours later the contents are aspirated, and a light pressure dressing is applied.

X-ray treatment.—F. M. Lyle, employing X-ray therapy, finds that a higher percentage of cures is obtained of ganglia of the wrist and hand by this method than by any other, and that scarring does not follow the treatment. The number of X-ray treatments depends on the size, duration, and previous treatment. Eight patients required 1 only, one received 7, and another, 8; the average number was nearly 3. The dosage employed was 1.5 erythema, given over the swelling. If one treatment did not effect disappearance of the swelling, a similar dose was given each month until cure was obtained. Of 21 patients so treated, 81 per cent were completely cured, 78 per cent of those complaining of pain were relieved, and 82 per cent of those complaining of weakness had a return of normal function in the joint.

- Ball, E. J. (1940) *Amer. J. Surg.*, **50**, 722.
 Lyle, F. M. (1941) *J. Bone Jt Surg.*, **23**, 162.
 Stecher, R. M. (1941) *Amer. J. med. Sci.*, **201**, 801.

HEADACHE

See also B.E.M.P., Vol. VI, p. 199; Cumulative Supplement, Key No. 618; and Surveys and Abstracts 1939, p. 363; 1940, p. 329.

Prognosis and Treatment*Ocular pain*

Retrobulbar injection of proctocaine.—L. H. Savin and T. M. Tyrrell employed retrobulbar injections of proctocaine in 18 cases of intractable ocular pain. Of these the pain was completely relieved in 11, and partially in 5. In 2 cases diplopia occurred after the injection, but rapidly passed off. There were not any toxic symptoms. The solution consisted of procaine 1·5 per cent, butyl-*p*-aminobenzoate 6 per cent, and benzyl alcohol 5 per cent in almond oil. The injection is given by the ordinary technique of retrobulbar injection. About 1 to 1·5 cubic centimetres of the solution is injected slowly inside the muscle cone in the neighbourhood of the ciliary ganglion.

Savin, L. H., and Tyrrell, T. M. (1940) *Brit. J. Ophthalm.*, **24**, 560.

HEART DISEASES: EXAMINATION

See also Surveys and Abstracts 1940, pp. 98 and 329; and pp. 2 and 44 of this volume.

Effort Syndrome*General review*

J. Parkinson lays stress on the psychological rather than on the cardiological factor in the effort syndrome. In war-time a large number of civilians change over to military life and atmosphere, and some, especially those who had symptoms of effort syndrome in peace-time, are upset by the shift. The part played by the nervous system, particularly in the realm of psychology, was recognized and has influenced treatment, but it was not sufficiently studied in the war of 1914–18. The tentative definition of effort syndrome given is 'a functional circulatory disease, most evident on exertion, unmasked or produced by war service'. It is rare in the Navy and the Royal Air Force. In the present war there has so far been a preponderance of the psychoneurotic type. The causes are often multiple and are considered under the headings of constitutional, psychoneurotic, infective, and myocardial degeneration. The symptoms are almost invariably multiple and include exhaustion, left mammary pain, palpitation, dyspnoea, dizziness, and faintness. Of the physical signs, tachycardia is the commonest and often the only one. The heart and blood pressure are normal. The exercise test has a limited but not a great value, if only because many patients with effort syndrome give a normal response. It is better called 'the pulse response test' as in the Royal Air Force, than the exercise tolerance test. The symptoms of effort syndrome are often grafted on those of organic heart disease. The differential diagnosis must be made from organic heart disease, angina pectoris (effort angina), pulmonary tuberculosis, hyperthyroidism, and hypertension. As regards prognosis, the first concerted research on effort syndrome was made at Hampstead in 1916, was conducted on the most 'typical' cases available, and the inferences were inapplicable to the majority. Later the prognosis improved, especially among those treated by medical reassurance, drill, and games. As regards treatment, rest in bed is absurdly out of place, medicine is anathema, and the period in hospital should be as short as possible. Prevention would be furthered if medical recruiting boards refused to accept weaklings of poor physique likely to become the subjects of effort syndrome. For war purposes a convenient term for this group would be 'potential effort syndrome'.

Aetiology

'Da Costa's syndrome.'—In his Goulstonian lectures (1941) at the Royal College of Physicians of London on 'The Aetiology of Da Costa's Syndrome' P. Wood recommends that the name 'effort syndrome' should be dropped in favour of 'Da Costa's syndrome', described under the title of the 'irritable heart in soldiers' by J. M. Da Costa in 1871 from experience in and after the North and South war in North America. Wood's conclusions are as follows. The signs and symptoms more closely resemble those of emotion, especially fear, than those of effort in the normal subject. The mechanism of the somatic manifestations depends upon central stimulation, not upon hypersensitivity of the peripheral autonomic system. The central stimulus is emotional, and is commonly the result of fear. The reaction becomes linked to effort by a number of devices, which include misinterpretation of emotional symptoms, certain vicious circular patterns, the growth of a conviction that the heart is to blame, consequent fear of sudden death on exertion, conditioning, and hysteria. Treatment in the Army is shackled by inability to remove the distressing environmental factors which have caused or have aggravated the breakdown; by the difficulty in establishing intimate contact with a patient who did not choose his medical confidant; by the duty of having to serve the State first, the patient second.

Clinical picture

The recruit's heart.—Writing on 'the recruit's heart', a wider problem than effort syndrome or Da Costa's syndrome (P. Wood), E. N. Chamberlain analyses statistics of 130 recruits referred by Medical Boards of the Ministry of Labour for special examination, such as radiological and electrocardiographical examination of the cardiovascular system. These cases fall into the following groups: (1) Murmurs without organic significance; a systolic

murmur without other grossly abnormal signs was found in 36 recruits who were recommended for full military duty. (2) Murmurs indicative of organic disease: (a) mitral disease, 23 cases in all, 9 of which were of mitral stenosis: the cases with a systolic murmur only were the most difficult to adjudicate upon; in all 15 men with a systolic murmur were recommended for a lower grading; (b) aortic disease, 5 of aortic regurgitation; (c) congenital heart disease. Though some cases of these two groups proved organic, patients with valvular disease may be capable of hard physical work, but they are on the whole unsuitable. (3) Hypertension in 7 instances was the main question; when the rise in blood pressure was moderate, e.g. up to 170 milligrams of mercury (systolic), further readings were advised before final grading; with much higher blood pressure or accompanied by radiological changes or considerable arteriosclerosis, a lower grading was recommended. (4) Effort syndrome; of 17 cases in this group, 9 were recommended for lower grading. Next to group 2 (systolic murmurs), these were the most difficult. (5) Abnormal rhythms: in 2 cases there was a history of paroxysmal tachycardia, and, although they did not present any signs of organic disease, they were regarded as unsuitable. Eight other men, shown clinically and electrocardiographically to be examples of harmless arrhythmias, chiefly extrasystoles, were recommended for full military service.

Personality types.—E. Wittkower, T. F. Rodger, and A. T. M. Wilson, as a result of investigation on 50 patients with effort syndrome, classify them into 5 personality groups as follows: (1) the George Washington-Calvin-Quaker type (20 soldiers characterized by an unusually keen sense of duty and by a rigid, superficial, and deep morality, with severe repression of their aggressiveness); (2) resigned 'grouzers' (11 soldiers, similar in structure, but less repressed in their aggressiveness); (3) open rebels (3 soldiers, similar in structure, but overtly over-aggressive); (4) men with inferior physique and obsessional drive (12 soldiers, similar in structure, endowed with inferior physique and struggling in vain against this handicap); (5) hysterical quitters (4 soldiers). The commonest precipitating factor was emotional strain. It is concluded that the effort syndrome is predominantly a disorder occurring in individuals of an unduly high and severe self-regard, and the importance of repressed aggression in most of the patients is emphasized.

Auscultation

Portable amplifier

A. L. Smith describes a compact portable instrument for amplifying and making permanent records of heart sounds. It aims at correction of the difficulties of hearing heart sounds due to their low frequency, low energy liberation, rapid pulse rate, thickness of the chest wall, and extraneous noises. The stethoscope is not considered adequate. The instrument described consists of a crystal microphone fitting by a rubber bell to the chest; movable loud-speaker (with selection control for low and high frequencies); recorder, amplifiers, and cutting head. Sounds are amplified during the recording, allowing adjustment and selection of frequencies. Records can be reproduced immediately at different speeds and amplified to be audible in an auditorium. Sub-audible murmurs can be detected. The author has recorded 500 disks of patients of from 6 weeks to 78 years old and of 58 foetal hearts from 5½ months to maturity. A permanent record of heart sounds over a period can thus be kept. As heart sounds can be amplified direct from heart to speaker, the instrument is valuable in the examination of the foetal heart during delivery or maternal drug treatment, and of the hearts of patients under operation, and in clinical demonstrations.

Functional Capacity and Hypertension

Electrocardiographic investigation

T wave inversion.—S. Schnur, with a view to correlation of T wave inversion and the size and functional capacity of the heart, investigated 100 consecutive hypertensive subjects of both sexes and all ages; 5 of them were classified as malignant hypertension; there was evidence of over-digitalization in 4 and of recent coronary occlusion in 5. It was found that there is a positive correlation between the size of the heart and functional capacity. As the heart in hypertension enlarges, the T wave becomes progressively inverted in leads I and II, and upright in lead III. Left ventricular preponderance is a characteristic electrocardiographic pattern occurring in 35 per cent of patients with an enlarged left ventricle. It occurs with increasing frequency as the heart enlarges, and is characterized by left axis deviation, inversion of T, or of T₁, and T₂ with T₃ upright, and a depressed RS-T segment in lead I or in leads I and II and a raised RS-T segment in lead III. Since functional capacity and cardiac size are both directly related to left ventricular preponderance it is possible to estimate, with some degree of accuracy in many cases, the functional capacity and approximate size from the electrocardiographic picture. Because depressed RS-T segments in leads I and II and elevated RS-T in lead III are found in 35 per cent of enlarged hypertensive hearts, and this deviation is one of the cardinal patterns of posterior coronary occlusion, great care must be taken in making the latter diagnosis on the cardiographic evidence alone. The origin of the RS-T take-off and the presence of Q waves are of value in the differential diagnosis. Hypertension was the cause of left ventricular preponderance in 82 and syphilis in 15 of the 100 hypertensives. There was not any positive correlation between the level of the blood pressure and the above changes; the data available do not solve the problem of whether the duration of hypertension, enlargement *per se*, or some other factor associated with enlargement is

responsible for the T and RS-T changes. It is not thought that the few cases of coronary occlusion or over-digitalization among the hypertensives affected the general conclusions.

Chamberlain, E. N. (1941) *Brit. med. J.*, **1**, 354.

Parkinson, J. (1941) *Brit. med. J.*, **1**, 545.

Schnur, S. (1941) *Brit. Heart J.*, **3**, 30.

Smith, A. L. (1941) *Med. Times*, N.Y., **69**, 243.

Wittkower, E., Rodger, T. F., and Wilson, A. T. M. (1941) *Lancet*, **1**, 531.

Wood, P. (1941) *Brit. med. J.*, **1**, 767, 805, 845.

HEART DISEASES: CONGENITAL DISEASES

See also B.E.M.P., Vol. VI, p. 206; Cumulative Supplement, Key Nos. 619–635; Surveys and Abstracts 1939, p. 364; 1940, p. 331; and p. 2 of this volume.

Dextrocardia

Complete situs inversus

Visceral pain.—A. B. King collected 79 cases of complete situs inversus, with visceral pain due to appendicitis, cholecystitis, or cardiac disease. To this list he adds 2 more instances of cardiac pain and 1 of pain from acute appendicitis. There was also a case of peptic ulcer. Since many of those patients apparently had a paradoxical distribution of pain as compared with the position of the affected organ, King suggests that the peripheral nervous routes may, or may not, be transposed independently of the viscera, the rotation occurring in about 50 per cent of the cases. When the transposition does occur, both viscera and pain patterns are reversed, whereas in cases of non-rotation of the nervous pathways the pain pattern remains in its usual location, although the viscera are transposed.

Right-sided Aortic Arch

Clinical picture

Radiology.—A. Hope Gosse records the case of a man, aged 56 years, who for more than 50 years had not suffered in any way from the presence of this developmental abnormality. In February 1940 he had an attack of right-sided pleurisy which was regarded as due to a malignant mediastinal tumour. Treatment by X-rays was then under consideration. He had been examined 4 years previously for irregularity of the heart and the full records then made were available; these showed that the radiological appearances on the two occasions were identical, thus ruling out the provisional diagnosis of malignant disease in the mediastinum. On reviewing the medical history after the diagnosis of a right-sided aorta had been established, the only relevant symptom was the occasional regurgitation of unchanged food. An electrocardiogram taken in 1936 showed the left ventricle preponderance so common in the middle life, and no abnormal features.

Heart-Block

Clinical picture

Adams-Stokes attack and the electrocardiogram.—Adams-Stokes disease is a name applicable to patients with heart-block who suffer from recurrent attacks of loss of consciousness due to ventricular stand-still, ventricular tachycardia, ventricular fibrillation, or a combination of these. During an Adams-Stokes attack from ventricular stand-still the auricle continues to beat, whereas in cardiac syncope of other types there is as a rule total cardiac stand-still. Cardiac syncope of neurogenic origin (e.g. ordinary fainting, and ventricular stand-still from disease affecting the vagus or carotid sinus) and cardiac syncope of myocardial origin without heart-block (e.g. in nodal bradycardia and in paroxysmal ventricular tachycardia) are excluded by this definition, although there are borderline cases. The cardiac mechanism of Adams-Stokes attacks was studied by Parkinson, Papp, and Evans on electrocardiograms recorded during the period of unconsciousness, in 64 cases. These fall into four groups or types and are tabulated according to the electrocardiographic basis of the attack, as follows: group 1 includes those with ventricular stand-still alone; group 2 includes both those with (a) low ventricular tachycardia and (b) high ventricular tachycardia and fibrillation, when either is followed by ventricular stand-still; group 3 includes those with the high ventricular tachycardia and fibrillation without ventricular stand-still; group 4 includes those rare cases with extreme bradycardia in heart-block. It is evident that ventricular stand-still alone is not the only cardiac lapse which determines an Adams-Stokes attack. It is often due to ill action, not to inaction, of the ventricle. Ventricular stand-still is responsible for about 55 per cent, ventricular tachycardia (with or without ventricular fibrillation), followed by ventricular stand-still, for 25 per cent, and ventricular tachycardia without ventricular stand-still for 20 per cent. Ventricular stand-still is sometimes consecutive to a rise in the auricular rate. As exertion or emotion so seldom determines ventricular stand-still, this increase in the auricular rate probably originates locally in the auricle and not from any nervous influence. During a short ventricular stand-still (below 20 seconds) the auricle beats regularly, often at an increasing rate, and the persistence of P waves during the ventricular stand-still is a feature distinguishing it from the total stand-still of cardiac syncope. During a long ventricular stand-still (above 20 seconds), or when ventricular stand-still is preceded by high ventricular tachycardia and fibrillation (group 2), the auricle may show slower, irregular, and ectopic P waves, auricular fibrillation and flutter, or it may even stop. In the group with ventricular

tachycardia, multiple and variable extra-systoles and varying bundle-branch block complexes between the attacks are common, as might be expected. Low ventricular tachycardia (up to 160) does not produce unconsciousness, but it provokes the subsequent ventricular stand-still which does produce—group 2 (a). High ventricular tachycardia and fibrillation (200–500) produce unconsciousness—group 3—and this may be prolonged by the subsequent ventricular stand-still—group 2 (b). The electrocardiogram of ventricular tachycardia is composed of regular deflections like bundle-branch block, which at high rates merge into simple undulations; yet the term 'ventricular flutter' need not be used, for the resemblance to auricular flutter is superficial. Ventricular fibrillation is distinguished from ventricular tachycardia by its irregularity in both rate and form, although the rate per minute may be the same, higher, or even lower. High ventricular tachycardia easily passes into fibrillation, which ends with ventricular stand-still or with gradual resumption of the basic rhythm through a period of low ventricular tachycardia or of varying extrasystolic complexes. The essential basis of an attack can be decided only by electrocardiogram. The prolongation of unconsciousness or its late onset in ventricular tachycardia and fibrillation cannot distinguish this group from that of ventricular stand-still alone, because other factors may influence unconsciousness, e.g. the suddenness of the development of block or of the fall in rate, a rapid succession of attacks, and the state of the cerebral arteries. For similar reasons it is difficult to state exactly what must be the duration of the circulatory arrest to produce syncope or convulsions. In established complete heart-block or in partial heart-block the Adams-Stokes attack may belong to any group, whereas in paroxysmal heart-block it is generally in group 1, i.e. ventricular stand-still alone. After coronary thrombosis, attacks due to ventricular stand-still alone may occur, as well as those due to ventricular tachycardia and fibrillation. Prognostic significance cannot be attached to the grade of heart-block, partial or complete, obtaining between the attacks, but the electrocardiographic nature of the attack has great significance in prognosis—and doubtless in treatment, although this is not here considered. Patients with ventricular stand-still (group 1) have a fair chance of recovery and often survive for many years, whereas those with ventricular tachycardia and fibrillation (groups 2 and 3) seldom recover, and if they do they rarely survive for more than a year.

Patent Ductus Arteriosus

Clinical picture

Left ventricular compensation.—E. C. Eppinger, C. S. Burwell, and R. E. Gross, as a result of a study of the circulation in 6 patients before and after surgical closure of an uncomplicated patent ductus arteriosus, state that (1) when the ductus arteriosus is open, the blood flow is from the aorta to the pulmonary artery. These patients are not cyanotic. (2) The volume of blood flowing from the aorta to the pulmonary artery varies from 4 to 19 litres per minute, i.e. 45 to 47 per cent of all the blood pumped into the aorta by the left ventricle. (3) The left ventricle expels from 2 to 4 times the output of blood from the right ventricle in a given period of time. (4) Adjustment of the circulation to the patent ductus arteriosus may be made by an increase in the output of the left ventricle. If this is not sufficient to compensate completely for the leak through the ductus, there may also be a diminution in the flow of blood to the periphery.

Surgical treatment

Indications.—R. E. Gross states that surgical treatment of patent ductus arteriosus should be advised only in carefully selected cases. He believed that complete obliteration of the vessel could not be accomplished in all cases by ligation, and therefore that all cases of the anomaly should not be operated on in the hope of preventing subacute bacterial endocarditis. Experience of 10 cases showed that ligation produced excellent results when used for patients with retarded physical development or evidence of cardiac embarrassment. If a procedure could be evolved by which the ductus arteriosus could be completely and safely severed, it would be justifiable to employ the operation more extensively in order to diminish the incidence of *Streptococcus viridans* infection. Whether ligation would diminish the incidence of subacute bacterial endocarditis is doubtful. It is technically possible to perform this operation at any age, but it is best to delay it until the patient is 5 or 6 years old. The results of operation appear to be better if it is performed in the childhood period.

Defects of the Interauricular Septum

Clinical picture

Importance of radiology.—D. E. Bedford, C. Papp, and J. Parkinson point out that patent foramen ovale and atrial (auricular) septal defect (A.S.D.), though both characterized by an aperture in the atrial septum, are embryologically and pathologically different conditions. Slit patency of the foramen ovale, to a probe or even a pencil, occurs in 20 to 30 per cent of all necropsies; as it should close during the first year of life, it is rather an anatomical variation of a pre-existent condition than a congenital cardiac lesion. Terminal cyanosis and paradoxical embolism are the only two events, and they are rare, referable to this common condition of a slit or widely patent foramen ovale. Quite different is the true congenital, and the commonest congenital defect, of the atrial septum; it is often associated with other congenital cardiac defects, such as defect of the ventricular septum and pulmonary stenosis. It is the only congenital lesion that occurs at all often in association with mitral stenosis; rheumatic cardiac lesions are often seen, but subacute bacterial endocarditis, commonly implanted on

effusion. They do not influence the course of rheumatic infection or that of rheumatic endocarditis and myocarditis. In one case 150 to 200 grains of salicylate were given daily for 11 days.

Boas, E. P., and Ellenberg, M. (1940) *J. Amer. med. Ass.*, **115**, 345.

HEART DISEASES: MYOCARDIUM DISEASES

See also B.E.M.P., Vol. VI, p. 277; Cumulative Supplement, Key Nos. 638-641; and Surveys and Abstracts 1939, p. 367; 1940, p. 333.

Myocarditis

Myocardial infection

Pain in shoulder as sequel.—A. C. Ernstene and J. Kinell record 17 cases (13 males, 4 females) among 133 consecutive cases of myocardial infection, of persistent pain in one or both shoulders. The average age of the 17 patients was 54 years and was slightly lower in the 4 females. The severity of the infection ranges from the clinical picture of typical peri-arthritis with intense pain and great limitation of movement to a mild aching pain with a sensation of weakness but without loss of function. The left shoulder is affected more commonly than the right. The pain persists for less than 3 months to more than 2 years. In 6 patients changes similar to those of chronic arthritis develop in other joints either simultaneously with, or subsequent to, the appearance of the shoulder symptoms. The pain in the shoulder region has been ascribed to radiation of the anginal pain to a shoulder already the site of slight pain; or it may be that different pain impulses from the heart sensitize the neurons, the fibres of which join the brachial plexus (Boas and Levy). The authors suggest that the pain may be the result of relative disuse of the shoulder and abnormal tension of the muscles of the shoulder girdle, some patients unconsciously keeping these muscles on one or both sides tense as a protective mechanism against pain.

Clinical picture

Cardiac infarcts.—A. M. Master, R. Gubner, S. Dack, and H. L. Jaffe report that fluoroscopic examination in 80 patients with cardiac infarcts secondary to coronary occlusion revealed abnormalities in the contraction of the left ventricle in 59, or 73 per cent. This was evident as a localized impairment of pulsation along the left ventricular border which was best observed in the ordinary posterior-anterior view, and most often in the apical, and particularly the supra-apical, region. The abnormalities consisted of complete reversal of pulsation (29 cases), partial reversal (11 cases), absence of pulsation (2 cases), and marked localized diminution of pulsation (17 cases).

Wounds of the Heart

Clinical picture

Bullet lodged in heart.—G. Grey Turner records the case of an officer who, in April 1917, when 32 years of age, was hit by a bullet from a machine-gun firing about 500 yards off, on the front of the left chest half an inch below and a quarter of an inch outside the left nipple. Radiologically there was a service bullet with its base anchored probably near the tip of the left ventricle and moving with it, and its point whirling about in the blood vortex in the cardiac cavity. As the risk of detachment of a foreign body in the heart and forming an embolus seemed serious, operation was thought advisable. The pericardium was opened, but in spite of a careful operation lasting 1½ hours, the search was abandoned because the bullet could not be located and it was regarded as inadvisable to prolong it by opening the cardiac cavities. It might have been near the base of the interventricular septum; for when mild pressure was applied to this area, the heart ceased to beat. The patient, however, bore the operation well and left hospital after 9 weeks able to resume his work. In April 1941 he was very well and free from any cardiac disability, and with a normal electrocardiogram. A radiogram showed the bullet embedded in the wall of the left ventricle.

Boas, E. P., and Levy, H. (1937) *Amer. Heart J.*, **14**, 540.

Ernstene, A. C., and Kinell, J. (1940) *Arch. intern. Med.*, **66**, 800.

Master, A. M., Gubner, R., Dack, S., and Jaffe, H. L. (1940) *Amer. Heart J.*, **20**, 475.

Turner, G. G. (1940) *Lancet*, **2**, 487, and an expanded account (1941) *Surg.*, St. Louis, **9**, 832.

HEART DISEASES: ENDOCARDITIS, MALIGNANT

See also B.E.M.P., Vol. VI, p. 297; Cumulative Supplement, Key Nos. 644-646; Surveys and Abstracts 1939, p. 368; 1940, p. 334; and p. 2 of this volume.

Subacute Bacterial Endocarditis

Aetiology

After syphilitic aortic valvulitis.—E. Libman in 1917 commented on the rarity of the incidence of subacute bacterial endocarditis on aortic valvular change due to syphilis. D. H. Rosenberg in a review of this subject adds 7 proved cases of the implantation of the lesions of subacute bacterial endocarditis on a pre-existing syphilitic aortic valve, and in a critical survey of the reported cases finds that in 7 cases this sequence of events held good, and that in 3 more the endocarditis was acute, making 10, and with his own cases, 17; whereas in 33 other cases so described the evidence did not seem satisfactory. Contrary to current opinion it appears

that bacterial endocarditis associated with syphilitic lesions of the aorta, without involvement of the aortic cusps, is not rare. The striking contrast between (i) the comparative frequency of subacute bacterial endocarditis supervening on rheumatic (mitral) valvulitis and (ii) the same sequence of subacute bacterial endocarditis and syphilitic valvulitis (aortic) has given rise to several hypotheses: syphilis and rheumatic infection are both common, but the age incidence might render the opportunities for bacterial infection of a syphilitic cardiac lesion much shorter-lived than in the case of rheumatic valvulitis; or that rheumatic and streptococcal infection are closely related; or that rheumatic valvular lesions have a better vascular supply; or that syphilitic deformity of the aortic valves results in diminished excursions of the cusps, thereby providing smaller areas for the settling of bacteria.

Clinical picture

Atypical verrucous endocarditis combined with lupus erythematosus.—At the time of his death in 1937 in an aeroplane accident L. Gross, director of the laboratories at the Mount Sinai Hospital, New York, left his observations on the cardiac condition in 23 fatal cases of acute disseminated lupus erythematosus and compared them with 4 cases of the atypical verrucous endocarditis, described by E. Libman and B. Sacks in 1924, with lupus erythematosus. He also left, it was believed, further material on this subject to be incorporated in this paper, and this paper has been delayed in the hope that this might be done; but no such revised copy has been found, and accordingly the article has now been published in its present form. Libman and Sacks described a clinico-pathological syndrome based on 4 cases presenting resemblances to both rheumatic fever and subacute bacterial endocarditis; 2 of their cases showed characteristic lesions resembling acute lupus erythematosus. In 1931 G. Baehr reported 17 cases of non-rheumatic verrucous endocarditis, including the 4 cases of Libman and Sacks, in 10 of these 17 cases there was the butterfly-shaped facial lesions of lupus erythematosus, and in 12 cases an extensive erythema on the upper part of the chest anteriorly and on the elbows, knees, and external surfaces of the legs and arms. In 1935 G. Baehr, P. Klemperer, and A. Schiffrin recorded 23 cases of acute disseminated lupus erythematosus examined after death, with a non-rheumatic verrucous endocarditis in 13, and vascular lesions in the kidneys in 18 cases, 5 of which showed similar vascular lesions in many other organs. Gross gave in his paper a detailed account of the cardiac lesions in (a) 23 fatal cases of acute diffuse lupus erythematosus, 18 from Baehr, Klemperer, and Schiffrin and 5 more recent cases, and (b) 4 hearts from cases of atypical verrucous endocarditis without any evidence of lupus erythematosus. In 5 and possibly 7 of the 23 cases there were signs of rheumatic endocarditis, but the cardiac lesions of atypical verrucous endocarditis and acute lupus erythematosus are alike and differ from those of rheumatic infection. Among the 23 cases there were characteristic naked-eye lesions of atypical verrucous endocarditis, and in all microscopic lesions were present. With regard to the relation between atypical verrucous endocarditis and acute diffuse lupus erythematosus Gross wrote that the common denominator appeared to be the clinical features described by Libman and Sacks, the cutaneous manifestations of diffuse lupus erythematosus being often, but not always, present. It was therefore suggested that the two groups should be placed into the single category of Libman-Sacks disease.

Streptococcus viridans infection with recovery.—Parkes Weber reports a case of recovery from subacute bacterial endocarditis in a man aged 52. The blood culture was positive for *Streptococcus viridans*, and he presented all the signs of the disease. Nevertheless his condition improved. He then had an attack of coma, with left hemiplegia, apparently due to right cerebral embolism. Since this attack of embolism, in August 1940, there had, at the time of the report, been no signs of active bacterial endocarditis. Sulphonamide therapy was not employed.

Effects on nervous system.—E. C. Toone, Jun., states that the fundamental pathological change in the central nervous system in cases of bacterial endocarditis is a diffuse embolic meningo-encephalitis from which the various clinical manifestations ensue. Although the clinical neurological manifestations are not entirely predictable, they follow a broad pattern, which includes meningitis, the most frequent, hemiplegia, subarachnoid haemorrhage, psychosis, and aphonia. The presence of a 'sterile meningitis' in any case of an obscure febrile illness should suggest the possibility of a viridans endocarditis.

Meningococcal infection without meningitis.—M. G. Whillans records a case of subacute meningococcal endocarditis and myocarditis without meningitis in a woman aged 40. Up to the present time 20 such cases, 2 of them subacute, have been confirmed by necropsy; in 11 of the 20 cases the mitral valve alone was involved, and in 3 more both the mitral and aortic valves were affected. In about half of the 20 cases there was not any meningitis. The meningococcal infection in Whillans's case was implanted on mitral stenosis of rheumatic origin. On practically the whole of the auricular surface of the posterior flap of the mitral valve there was a very irregular, moderately firm, elastic mass of yellowish pink vegetations; there were similar but less extensive vegetations on the other segment of the mitral valve. Microscopically the vegetations consisted of irregular masses of platelets and reticular fibrin showing various degrees of organization; several almost completely organized masses were covered by endothelium. Throughout the vegetations there were patchy aggregations of neutrophils with fewer lymphocytes, and among them were small greyish masses of myriads of intracellular and extracellular meningococci. The myocardium showed cloudy swelling and old patches of fibrosis of rheumatic origin, but no evidence of recent rheumatic activity. The arterioles in

the myocardium contained rounded granular masses, almost, but never completely, occluding the lumen. These plugs, usually covered by a single layer of endothelium, varied (a) in their appearance, but did not contain fibrin, and (b) in the degree of inflammatory reaction. Similar changes in many of the smaller arteries and arterioles of the pancreas, liver, adrenals, and uterus were found. Three possible explanations—namely, embolism, thrombosis, and medial necrosis due to bacterial toxins—are discussed, the last being regarded as most attractive. Although these unusual lesions of the arterial tree are spoken of here as unique, reference is made to the observations on the changes—arteritis verrucosa and granular plugged vessels—in the coronary arteries in rheumatic fever; the arteritis verrucosa occupies an intermediate position between a necrotizing arteritis and granular plugged vessels, whereas granular plugged vessels are, it is suggested, due to proliferation of the vascular endothelium with swelling and granular transformation of the protoplasm, fusion of the cells, and degeneration of the nuclei. These changes, described by L. Gross, M. A. Kugel, and E. Z. Epstein, do not show the acute inflammatory reaction seen in the meningococcal form.

Treatment

Sulphapyridine.—J. G. Macleod records the case of a man, aged 20 years, with a rheumatic history and a cardiac lesion of 7 years' duration. His blood gave a profuse culture of *Streptococcus haemolyticus*, the urine contained albumin and red blood corpuscles, and there were apical systolic and basal systolic and diastolic cardiac murmurs. He received a total of 241.5 grammes of sulphapyridine and showed remarkable improvement: the anaemia diminished, some of the Osler's nodes disappeared, and 4 successive blood cultures were negative. The case is unusual in being due to a haemolytic streptococcus rather than *Streptococcus viridans*, and it is suggested that the sulphapyridine destroys the haemolytic streptococcus more easily than it destroys *Streptococcus viridans*. The author collected 8 other cases treated with sulphapyridine; these gave more encouraging results than were obtained in a collection of 14 cases of subacute bacterial endocarditis treated by combined sulphapyridine and heparin.

Heparin.—C. M. Fletcher states that the heparin treatment of subacute bacterial endocarditis entails the risk of causing cerebral and other vascular accidents. He reports a case in which heparin treatment was adequately maintained for 14 days, the patient then dying of cerebral haemorrhage. At necropsy the cardiac vegetations in no way differed from those seen in untreated cases.

Sulphapyridine and heparin.—C. M. Fletcher also tried using sulphapyridine and heparin in a case of subacute bacterial endocarditis. The patient died of cerebral haemorrhage. The object of heparin therapy in such cases is, according to S. R. Kelson and P. D. White, to restrict the nidus and culture field for bacterial growth, to prevent embolism from the freeing of fresh thrombi, and to check the growth of the vegetations so that proliferating fibroblasts may fill in the area thus limited. At the same time, and for a week before and after the 14 days of heparin treatment recommended, sulphapyridine is given for its bacteriostatic action. S. Seviitt reports 2 cases of bacterial endocarditis treated with heparin and sulphapyridine. One patient died from pulmonary embolism and the other from cerebral embolism. In one case there was a rapid clinical improvement during treatment and the valvular vegetations were very much smaller than is usual and contained less fibrin. The author concludes that, though the treatment is undoubtedly highly dangerous, it seems to be justifiable for what otherwise is invariably a fatal disease.

Bacteriology and treatment

In *Streptococcus viridans* types.—A. C. DeGraff analyses the present position of the treatment of subacute bacterial endocarditis, strictly confining his material to cases proved to be due to the presence of the *Streptococcus viridans* and of clinical evidence of cardiac disease, and not considering cases so described, but due to other and haemolytic streptococci, staphylococci, and gonococci. DeGraff has not cured a case, but he quotes E. Libman's experience of 25 cures, or 3 per cent. It has been suggested that the disease has become more virulent since 1924, but Libman does not agree with this view. It should be regarded as an infection characterized by masses of bacteria growing in fibrin, suspended in and yet isolated from the blood stream. Treatment other than by sulphonamides is briefly given, with the initial comment that probably no disease has had so many remedies and that this alone shows the futility of most of them. J. A. Capps reported 4 cures with sodium cacodylate, but could not repeat this success; and among 250 collected cases S. R. Kelson found no benefit from arsenicals. The sulphonamides have been extensively used; among 120 patients treated with sulphanilamide, P. Long had 5 recoveries in his first 50 cases but none in the subsequent 70 cases. The 5 patients who recovered were all in as good health as their underlying cardiac condition would allow them to be, and this for an average of 2½ years without any recurrence. Other results are quoted. An important question is the penetration of drugs through the fibrin to reach the bacteria on the cardiac valves; sulphanilamide, sulphapyridine, and sulphathiazole cannot do this; but an ingenious attempt to overcome this has been made in the addition of heparin to sulphapyridine, and thus to arrest the deposition of platelets and fibrin. Few observers have identified the strains of the *Streptococcus viridans*, but there is experimental evidence that the identification of the particular strain is important as regards virulence; H. Fox investigated the relation of strains of the green streptococcus to 4 different clinical groups of the disease. In general it may be said that the slower the clinical course the more likely is the micro-organism to be of non-human type. It is quite possible that one

form of drug is effective for one strain, another for a different one. Although this review does not show any very encouraging feature immediately, the therapeutic problems are being investigated scientifically.

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 — (1941) *ibid.*, **1**, 444.
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 Gross, L. (1940) *Amer. J. Path.*, **16**, 375.
 — Kugel, M. A., and Epstein, E. Z. (1935) *Amer. J. Path.*, **2**, 253.
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 Libman, E. (1917) *M. Clin. N. Amer.*, **1**, 573.
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 — and Sacks, B. (1924) *Arch. intern. Med.*, **83**, 107.
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 Rosenberg, D. H. (1940) *Arch. Intern. Med.*, **66**, 441.
 Seviitt, S. (1941) *Lancet*, **1**, 443.
 Toone, E. C., Jun. (1941) *Ann. intern. Med.*, **14**, 1551.
 Weber, F. P. (1941) *Lancet*, **1**, 630.
 Whillans, M. G. (1940) *Amer. J. Path.*, **16**, 365.

HEART DISEASES: MITRAL VALVE DISEASES

See also B.E.M.P., Vol. VI, p. 309; and Surveys and Abstracts 1939, p. 369; 1940, p. 336.

Mitral Stenosis

Morbid anatomy

Ball thrombi.—C. F. Garvin records 3 ball thrombi in 156 consecutive necropsies in cases in which rheumatic heart disease was the chief, or an important contributory, cause of death. Rheumatic mitral stenosis with auricular fibrillation was present in all 3 cases. The ball thrombi were the cause of attacks of syncope to which 2 of these patients were subject. The third patient died suddenly. At necropsy a smooth ovoid-shaped thrombus was found wedged in the stenosed mitral orifice.

Garvin, C. F. (1941) *Amer. Heart. J.*, **21**, 371.

HEART DISEASES: AORTIC VALVE DISEASES

See also B.E.M.P., Vol. VI, p. 329; and Surveys and Abstracts 1939, p. 370.

Diagnosis

Functional aortic insufficiency

Systolic pressure in upper and lower extremities.—According to S. A. Loewenberg, in functional aortic insufficiency the systolic pressures in the upper and lower limbs are about equal, whereas in organic aortic insufficiency (as L. Hill, M. Flack, and W. Holtzmann showed in 1910) the systolic pressure in the lower limb is from 50 to 100 millimetres, or more, higher than in the arms. This constitutes a valuable diagnostic sign in functional aortic insufficiency.

Hill, L., Flack, M. and Holtzmann, W. (1909–10) *Heart*, **1**, 73.

Loewenberg, S. A. (1941) *Ann. intern. Med.*, **14**, 991.

HEART DISEASES: RIGHT SIDE DISEASES

See also B.E.M.P., Vol. VI, p. 357; and Cumulative Supplement, Key Nos. 653–658.

Hypertrophy

Clinical picture

Subacute cor pulmonale.—D. G. Mason refers to (1) the acute form or cor pulmonale practically confined to pulmonary embolism and rarely associated with right ventricular hypertrophy, and (2) the chronic primary form of cor pulmonale which includes stenosis and incompetence of the pulmonary valves, pulmonary endarteritis, organic tricuspid insufficiency, mitral stenosis, diffuse fibrosis of the lungs, and pulmonary emphysema. Mason reports a case in a woman aged 65, of the subacute form, of which a case was described by I. C. Brill and T. D. Robertson who referred to 2 cases previously recorded; these 3 cases were all due to carcinomatous metastases in the pulmonary arterioles. The subacute form is characterized by a fairly rapid (9 days to 2 months) development and termination of signs and symptoms of strain of the right side of the heart in patients without any history of previous cardiac or pulmonary disease, and by moderate enlargement and dilatation of the right side of the heart. At necropsy there were a few isolated discrete metastatic carcinomatous nodules under the surface of the left lobe of the liver, and a secondary growth in the frontal bone. Microscopical examination of the lungs showed that the small branches of the pulmonary arteries and arterioles contained solid nests of carcinomatous cells which in most instances com-

pletely filled and plugged the vessels. The right mamma had been removed for carcinoma 19 months before death. Mason refers to 2 cases reported by K. Maddox as subacute cor pulmonale, but does not accept them.

Brill, I. C., and Robertson, T. D. (1937) *Arch. intern. Med.*, **60**, 1043.

Maddox, K. (1939) *Med. J. Aust.*, **1**, 18.

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HEART DISEASES: HEART FAILURE

See also B.E.M.P., Vol. VI, p. 368; Cumulative Supplement, Key No. 659; Surveys and Abstracts 1939, pp. 20, 59, and 370; 1940, p. 337.

Clinical Types

Congestive heart failure

Prognosis.—Seven hundred and forty-eight patients with congestive heart failure were analysed by N. H. Boyer, C. E. Leach, and P. D. White. Prognosis was found to depend less on the underlying form of disease than on the precipitating causes of failure; these include complicating factors, age, and cardiac enlargement. The complicating factors with the poorest prognosis were hypertension, infections, anaemia, surgical operations, pulmonary malignant disease, bronchial asthma, pregnancy, pulmonary infarction, coronary thrombosis, and rheumatic fever. Patients with hypertension are known to have a poor prognosis for congestive heart failure, but in the patients under review the proportion which did badly was equal in the hypertensive and hypotensive patients, when once failure had set in. Blood pressure falls were observed in 83 per cent of the known hypertensives, and in 50 per cent of the hypotensives, the fall in most cases being to normal or below. It is concluded that it is the fall and not the level of blood pressure that is significant in congestive failure. Age is important in prognosis. Prognosis was worst in the age groups 1–10, 41–50, and 71 onwards. There was usually a direct relation between cardiac enlargement and failure; out of 277 cases the majority had enlarged hearts. The prognosis was most favourable in those with only slight cardiac enlargement.

Treatment

Drugs

Mercurial diuretics.—Certain mercurial diuretics were submitted by W. Evans and T. Paxon to a clinical trial in 50 patients with heart failure, for the purpose of deciding their relative diuretic potency. The best method of administering them was also investigated, as well as the best means of augmenting their natural diuretic action. Esidrone, mersalyl, neptal, and salyrgan were given in doses of 2 cubic centimetres intravenously (197 times) and intramuscularly (110 times). Mersalyl, neptal, and salyrgan were tried orally in tablet form, and novurit and salyrgan were tested as a rectal suppository. Eleven methods of enhancing the diuretic effects of mercurial salts were also tested, and 507 observations were devoted to this problem. The results of this investigation are as follows. Neptal and esidrone when given intravenously or intramuscularly produced the largest diuresis, rather larger than salyrgan and much larger than mersalyl. The intravenous method almost always induced greater diuresis (average diuretic index of 76) than the intramuscular method (average diuretic index of 56). Of the two rectal suppositories tried, novurit gave much better results than salyrgan. Neptal tablets by mouth proved more efficient (average diuretic index of 32) than mersalyl tablets (average diuretic index of 19), salyrgan tablets, or novurit suppositories rectally (each with a diuretic index of 17). Ammonium chloride was always given in association. Although the urinary output after oral administration of a mercurial salt was greatest when 0.48 gramme (3 new tablets) of neptal was used, satisfactory diuresis was also produced by 0.32 gramme (2 new tablets). Thirty grains (2 grammes) of ammonium chloride given two hours before the administration of a mercurial preparation proved to be the best form of premedication. Enteric chocolate-coated tablets, each containing 7.5 grains (0.5 gramme), proved the most convenient form of dispensing ammonium chloride. In a patient confined to bed with heart failure and especially with oedema, standard treatment would include the injection of a mercurial diuretic (2 cubic centimetres) intravenously or intramuscularly every third day, preceded on each occasion by the administration of 4 tablets (30 grains or 2 grammes) of ammonium chloride by mouth two hours before. During the ambulatory stage the patient should take neptal tablets (3 in all, or 0.48 gramme) twice weekly in the more severe case and once a week in the less severe case, after the same premedication, and receive an intravenous or intramuscular injection (2 cubic centimetres) at intervals according to need.

Medical therapy and general management

Under the title 'A Talk on the Philosophy of Convalescence', F. A. Willius deals with cardiac disease in the light of comparatively recent advances, especially of congestive heart failure and coronary thrombosis, treated respectively by diuretics and by complete rest. In many instances the practical results of modern treatment are prolongation of life and a more optimistic outlook rather than cure. A distinction should be drawn between treatment, or the use of drugs and agents either continuously or periodically, and management which includes the all-important scheme of individualized control of a patient whose activities are restricted; necessary rest periods are imposed, and dietary adjustment and other supervisions exercised, which the patient must understand so as to co-operate. The vast majority of cardiac

patients should be permanently under medical supervision. Patients with cardiac impairment have lost their cardiac reserve, and the object of management should therefore be to re-establish the cardiac reserve. Middle-aged patients often adapt themselves more contentedly than do young patients, whose plans for life have thus been prematurely interrupted, to a revision of their activities. It is always unwise for a medical practitioner to tell a patient the specified duration of his life, or to use threats of a speedy collapse if his advice is contested.

Ouabaine and digitalis

R. C. Batterman, O. A. Rose, and A. C. DeGraff describe a method of obtaining rapid digitalization in congestive heart failure by the simultaneous administration of ouabaine intravenously and digitalis leaf orally. The patients had varying degrees of failure and different forms of heart disease; their ages ranged from 28 to 79. Fifty-nine out of 60 patients improved after various intervals from 15 minutes to 24 hours, in most cases within 1 hour, and in most cases this was progressive. After the initial digitalization it was not difficult to establish the maintenance dose of digitalis leaf. The method was applicable to patients with normal sinus rhythm, as well as to those with auricular fibrillation. The dose of ouabaine was 0.5 milligramme (5 cat units), and of digitalis leaf 6 or 8 cat units, depending on the estimated oedema-free weight of the patient. After 24 hours the patient was placed on a daily maintenance dose of 1 to 2 cat units of digitalis leaf by mouth.

Vitamin B₁

O. J. Morehead reports a case of a severe acute attack of dyspnoea in a child aged 2½ years, which was apparently relieved at once by the hypodermic injection of 10 milligrams of thiamine hydrochloride (aneurine). During the attack the child was obviously in great respiratory embarrassment, since all the accessory muscles of respiration were in action without enough oxygen being supplied for talking or crying. The lips and finger nails were slightly cyanotic. Respirations were 70 per minute, and pulse about 160, but regular. The temperature was normal. About 8 months previously the parents had noticed that the child had occasional palpitation with periods of dyspnoea, not so severe as the attack reported. Four months before the attack the tonsils had been removed and, after this operation, the attack of palpitation had become more frequent and severe. Five minutes after the injection of vitamin B₁ the child was asleep, the respiratory rate fell to 50 per minute, and the pulse rate to 110. She slept for 4 hours, then was given about 12 milligrams of the vitamin by mouth, and slept for a further 4 hours. Next day the child appeared to be normal. Thereafter she was given a preparation of vitamin B complex daily by mouth, and her symptoms had not recurred at the time of the report. The author recommends that vitamin B₁ should be given by injection in all cases of acute heart failure, and suggests that it should be employed prophylactically before an operation, such as tonsillectomy, particularly if it is severe and there is evidence of cardiac weakness.

Calcium gluconate

N. Morris and A. S. Rogen report on the treatment of 10 patients with cardiac oedema with calcium gluconate in doses of 10 cubic centimetres of a 10 per cent solution, intravenously every day for several days. The drug had little immediate effect on the urinary output, but in 6 out of the 7 patients who had previously been on digitalis the diuretic effect of this drug was increased when given after a course of injections of calcium gluconate. In 9 out of 10 patients with cardiac oedema, injections of parathyroid hormone increased the diuretic action of mersalyl and digitalis.

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HEREDITY AND CONSTITUTION

See also B.E.M.P., Vol. VI, p. 452; and Surveys and Abstracts 1940, p. 339.

Inheritance in Twins

Tumours

Uniovular and binovular twins.—Madge T. Macklin has collected records of 109 pairs of twins in whom tumours have occurred either in one or both of each pair. In these there were 63 monozygous (uniovular) twins in whom the heredity is as identical as it can be in 2 human bodies, and 46 dizygous (binovular) twins. In the monozygous series both twins were affected in a higher percentage than in the dizygous series (66.6 and 20 per cent respectively), and with the same kind of tumour and at more nearly the same age than among the dizygous twins. When one twin only was affected, the time during which the second twin remained free was much longer in the dizygous than in the monozygous. Thus the average time during which the second twin remained free from tumour growth was 2 years and 1 month among the monozygous twins; whereas among the dizygous twins the average time during which the second twin remained free was 6 years. The data thus collected point to the conclusion that

heredity is a major factor in the determination of the site, the type, and the age of onset of tumours.

Macklin, Madge T. (1941) *Canad. med. Ass. J.*, **44**, 604.

HERNIA

See also B.E.M.P., Vol. VI, p. 470; Cumulative Supplement, Key Nos. 672–687; Surveys and Abstracts 1939, p. 372; 1940, pp. 12 and 339; and p. 14 of this volume.

External Abdominal Hernia

Aetiology

Associated hepatic disease and ascites.—M. D. Altschule states that the incidence of hernia is high in patients with hepatic cirrhosis and ascites, and occasionally symptoms referable to the hernia may cause the patient to seek medical advice. The author reports from cases in which the development of a hernia was the first indication of severe intrahepatic disease, or at least of ascites; in 2 cases the ascites was discovered only during herniorrhaphy.

Treatment

New operative technique for inguinal hernia.—W. L. Estes employed a technique of repair in inguinal hernia consisting of a fascia-to-fascia closure in the rectus sheath. This method was used in 394 cases, of which 22 were bilateral, out of a total of 416 herniae. Of the cases 317 were indirect, 80 direct, and 19 recurrent. The patients' ages ranged from 12 to 75. In the group of 271 indirect herniae there was only one recurrence, or 0.04 per cent, and in the direct group the recurrence rate was 2.77 per cent. In the recurrent group the recurrence rate was 17.6 per cent.

Cord transplantation in inguinal hernia.—W. F. MacFee makes a preliminary report on the repair of inguinal hernia with transplantation of the spermatic cord to the femoral canal. The operation was performed on 21 cases of primary hernia (13 direct, 4 indirect scrotal, 2 simple indirect, 1 combined direct and indirect, and 1 direct, indirect, and sliding combined). The ages of the primary group ranged from 45 to 72 years, the average being 57 years. In the recurrent group, 12 in number, there were 5 direct, 4 indirect, 1 indirect sliding, 1 indirect partly sliding, and 1 direct and indirect sliding. The ages of the recurrent group ranged from 37 to 67 years of age, the average being approximately 46 years.

End results of injection therapy.—L. Manoil reports the end results of the injection treatment of hernia in 123 patients, 92 per cent of whom were between the ages of 41 and 90. In 26 cases, or 16.4 per cent, there were recurrences, and 5, or 3.2 per cent, of these were treated by operation, making a total of 19.6 per cent of failures. In the 15 younger patients, between the ages of 11 and 40, there were no recurrences. There were no infections and no deaths. The author concludes that the injection treatment is the method of choice for older patients, provided that the hernia is reducible and can be comfortably maintained with a truss.

Types of hernia

Eventration.—O. T. Clagett and C. F. Dixon report a case successfully operated upon, in a full-term male infant, first seen 6 hours after birth. Under ether administered by the drop method, the sac, which was the size of an orange, contained the whole of the liver and about one-third of the small intestine. In order to return the liver it was necessary to divide the round ligament, and closure of the abdomen was difficult because there was hardly enough room for all the viscera previously in the sac. Although an exhaustive examination of the abdominal contents was not made at the laparotomy, no other congenital defect was seen. There is not any satisfactory explanation of the presence of the liver in the sac. Normal rotation had apparently taken place, the caecum and vermiform appendix being visualized in their normal position. In their commentary the authors point out that this condition, also called 'hernia in the umbilical cord' and 'amniotic hernia', is not a true hernia because the viscera contained in the sac have never been in the abdominal cavity, and have remained outside in their primitive position in the coelomic cavity since their development during the first few weeks of embryonic life; *eventration* would therefore be a better title. The condition is rather rare, especially the massive form in this instance. Probably not more than 300 cases have ever been recorded, 100 during the last 50 years. But the sac is often so small, or the infant is still-born, so that it is not brought to the notice of practitioners.

Altschule, M. D. (1941) *New Engl. J. Med.*, **224**, 351.

Clagett, O. T., and Dixon, C. F. (1940) *Proc. Mayo Clin.*, **15**, 433.

Estes, W. L., Jun. (1941) *Ann. Surg.*, **113**, 838.

MacFee, W. F. (1940) *Ann. Surg.*, **112**, 1071.

Manoil, L. (1940) *Arch. Surg., Chicago*, **41**, 114.

HERPES

See also B.E.M.P., Vol. VI, p. 513; and Surveys and Abstracts 1939, p. 373; 1940, p. 341.

Herpes Zoster

Aetiology

Association with chicken-pox.—L. Rosenberg and J. Rosenberg report a case of herpes zoster in a woman, and after the usual incubation period, chicken-pox appeared in her two children. After reviewing the experimental and clinical evidence on the possible causes of

herpes zoster and chicken-pox, the authors conclude that there is a common aetiology in these two diseases.

Clinical picture

Herpes zoster with paralysis.—A. B. Carter and J. B. W. Dunlop record 2 cases of loss of power after herpes zoster and give a commentary. The 2 cases were in women aged 73 and 53. In both the region of the right hip, thigh, and leg were affected and there was some subsequent muscular wasting. Lumbar puncture showed a pleocytosis which persisted for several months. There was not any evidence of the existence of diseases, such as disseminated sclerosis, tabes dorsalis, or compression of the spinal cord that may be associated with herpes zoster. Attention is directed to the view that in herpes zoster inflammation involves the posterior roots, the meninges, and the spinal cord as well as the cells in the posterior nerve root ganglia. R. G. Abercrombie records a case of herpes zoster with muscular paralysis and sensory disturbance in a man aged 68. The motor and sensory changes do not correspond with the distribution of peripheral nerves, and have not the character of a root syndrome. It is thought probable that the clinical manifestations were due to a diffuse inflammation of the spinal cord, almost entirely unilateral, involving both the motor and sensory regions of the lower lumbar and upper sacral segments and the root ganglion of the third sacral (the diffuse morbid changes of Lhermitte). J. D. Spillane found in a small outbreak of herpes zoster 1 case of facial (Bell's) paralysis combined with herpes zoster of the trigeminal nerve on the same side, the facial herpes preceding the trigeminal herpes by 5 days. Facial paralysis and hemiageusia were the only signs of involvement of the geniculate ganglion.

Aberrant vesicles.—S. M. Bluefarb and G. E. Morris found that 20 out of 30 cases of herpes zoster showed aberrant vesicles. The number of aberrant vesicles in each case varied from 5 to more than 30. They mainly occurred in elderly patients, on the chest, abdomen, and back. In 12 of the 30 cases the condition was gangrenous, and in 9 of these there were aberrant vesicles. In only 11 of the 18 cases without gangrenous lesions were there aberrant vesicles.

Treatment

X-ray of the spine.—The successful treatment of herpes zoster, especially the persistent post-herpetic pain, by X-ray exposures of the spinal ganglia, previously practised by J. M. Kechline, has been confirmed by P. McCombs, A. Tuggle, and C. M. Guion who treated 72 out of 123 (males 48, females 75) patients, with 56 cured, 4 improved, and 12 failures (6 males, 6 females), 11 of whom were more than 50 years of age. The remaining 51 of the 123 patients served as controls. Among the 123 patients 76, or 62 per cent, were more than 50 years of age. The treatment consisted of 200 roentgens daily or every other day, for 5 or 6 treatments, using 200 kilovolts through 1 millimetre of copper and 1 millimetre of aluminium filter at 50 centimetres distance in a 6 by 15 portal directly over the spinal root ganglia of the nerves involved. Patients tend to leave off the treatment after a few treatments because the pain is relieved and the skin lesions do not show any spread. It is important to give a full course of 1,000 to 1,200 roentgens. Patients should be warned that the symptoms may be exaggerated after the first treatment. The largest number of patients were treated within the first week of the disease: 21 had had symptoms for 1 to 3 days, 23 for 4 to 7 days, 11 for 8 to 14 days, 4 for 15 to 28, and the remaining 13 for more than a month, 5 of these being failures. The importance of early treatment is shown by a cure in 89 per cent of patients starting treatment within the first week as compared with a cure of 50 per cent among those delaying treatment for 2 weeks.

Anaesthetic infiltration.—L. Secunda, W. Wolf, and J. C. Price obtained relief of pain in 13 of 15 patients with acute herpes zoster by infiltration of the hyperalgesic areas with novocain, 0.5 to 2 per cent with or without adrenaline, or with nupercaine or benzocaine in oil. The duration of relief after the injection was generally from 1 to 30 hours, after which there was recurrence of pain. Seven of the 9 patients who received a combination of novocain and an anaesthetic in oil experienced permanent relief of pain.

Herpes Simplex

Clinical picture

Associated with arsenical dermatitis.—C. C. Thomas reports a case of an unusually extensive recurrent type of herpes simplex in a negress aged 26. The condition had occurred periodically since the age of 15. After an attack of arsenical dermatitis the attacks of herpes became more frequent and wide-spread, recurring at intervals of 1 and 2 weeks, and involving in the course of time the entire cutaneous surface, except that of the face, scalp, neck, forearms, and legs. Sometimes multiple groups of vesicles developed. Apparent cure followed the intracutaneous desensitization with autogenous blood taken at the height of an attack of herpes.

Treatment

Moccasin snake venom.—A. A. Fisher reports the use of moccasin snake venom in herpes simplex and found that it generally diminishes the number and intensity of attacks. The dosage was usually 0.2 cubic centimetre of a 1 in 3,000 dilution, given subcutaneously, followed a week later by a similar dose. The venom was also used in 4 cases of herpes proenitalis with equally good results.

Herpes labialis checked with spiritus vini rectificatus.—From personal experience R. F. Price finds that spiritus vini rectificatus applied to the area on the lip as soon as slight irritation is felt, or as soon as the first sign of a bleb appears, and repeated frequently for a few hours, usually entirely aborts the further development of herpes labialis. Possibly a similar applica-

tion of spiritus chlorformi is known to be effective for this trivial but annoying recurrence. It may be added that many years ago J. Hutchinson in his *Archives of Surgery* pointed out that small doses of liquor arsenicalis, which in larger doses may cause herpes zoster, may prevent the recurrence of febrile or simple herpes.

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 Thomas, C. C. (1941) *Arch. Derm. Syph., N.Y.*, **43**, 817.

HISTOPLASMOSIS

See also B.E.M.P., Vol. VI, p. 520; and Surveys and Abstracts 1940, p. 342.

Clinical Picture

A. E. Brown, F. Z. Havens, and T. B. Magath record the first diagnosed case of histoplasmosis at the Mayo Clinic and review this subject. The patient, a man aged 48, had been ill for 2 years before death and, as shown clinically and by necropsy, was the subject of granulomatous ulceration of the palate, pharynx, epiglottis, larynx, small and large intestine. Intracellular *Histoplasma capsulatum* was demonstrated. The close resemblance of this parasite to that of leishmaniasis has been pointed out by many workers, and it is not unlikely that some cases diagnosed as leishmaniasis have been examples of histoplasmosis. It is regarded as rare; since 1939, 21 cases have been reported. The infection is wide-spread and has been reported in Panama, the Philippines, Honduras, Java, Argentina, Brazil, and 14 in the United States. The treatment, mainly by antimony preparations, is unsatisfactory, and most of the patients have died.

Occurrence in an infant

W. A. D. Anderson, I. D. Michelson, and T. M. Dunn report a case of histoplasmosis in an infant aged 8 months, the twelfth case to be recognized in the United States and the fifth to occur in an infant under 1 year of age. The clinical picture consisted of fever, upper respiratory symptoms, transient diarrhoea, and, at the end, purpuric haemorrhages. Considerable enlargement of the spleen and liver, severe anaemia, leucopenia, and lymphocytosis were found. Sulphonamide therapy was ineffective. At necropsy there was extensive reticulo-endothelial hyperplasia, with large numbers of the parasitic fungus *Histoplasma capsulatum* in the cytoplasm of phagocytic cells. The parasite had caused chronic inflammation of the lungs, and in the colon the fungus was found in relation to small areas of ulceration. Hyperplasia of endothelial cells lining small blood vessels led to partial or complete occlusion of their lumen.

P. H. Rhodes, N. F. Conant, N. C. Durham, and L. R. B. Glesne report a case of histoplasmosis in a female infant aged 3 months. This is one of the recorded cases in infancy. (In 1939 A. L. Amolsch and J. H. Wax collected 10 cases in female infants.) Blood cultures were positive for *Histoplasma capsulatum* 24 hours before death.

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HODGKIN'S DISEASE

See also B.E.M.P., Vol. VI, p. 523; Cumulative Supplement, Key No. 691; and Surveys and Abstracts 1939, p. 375; 1940, p. 342.

Complication associated with brucella infection

N. B. Wise and M. A. Poston report the coexistence of brucella infection and Hodgkin's disease in 14 consecutive cases by the isolation of *B. melitensis* in cultures from the blood or lymphatic glands. Brucella was isolated in cultures from the blood or lymphatic glands only once from a much larger group of patients with diseases of the lymphatic glands, other than Hodgkin's disease. Although the data in this investigation do not establish an aetiological relationship of brucella to Hodgkin's disease, the authors suggest that the clinical course of the latter may be significantly influenced by brucella infection.

Respiratory Tract*Intrathoracic lesion*

L. F. Craver, R. R. Braund, and H. Y. Tyler review the recorded cases of intrathoracic Hodgkin's disease. It appears that lesions in the mediastinal and other lymphatic glands in the chest are much commoner than those arising in the substance of the lungs. Much the rarest intrathoracic lesion is that originating in the bronchial mucosa. The formation of cavities in the lymphadenomatous nodules in the lungs is rare; it varies from areas of central necrosis in small nodules to a cavity 'the size of a child's head'. In some instances the co-existence of tuberculosis has been excluded. It has been suggested that irradiation and infection are responsible for cavity formation. Tracheo-oesophageal fistula has been recorded in 3 cases, one of these being among the 224 proved cases at the Memorial Hospital for Cancer and Allied Diseases, New York, where the authors work; in this case there were also bilateral abscesses in the lungs, generalized Hodgkin's disease, great enlargement of the mediastinal lymphatic glands, diffuse involvement of both lungs, which showed a peribronchial infiltration, the spleen and liver. Among 28 cases examined after death at this hospital 21 showed pleuro-pulmonary lesions. Intrathoracic involvement appears to be more often reported in Hodgkin's disease than in leukaemia, lymphosarcoma, and mycosis fungoides. Those intrathoracic lesions may not give rise to ordinary physical signs or symptoms.

Clinical Picture*Respiratory tract*

Haemoptysis.—R. Charr and A. Wascolonis report a case of Hodgkin's disease in which the lesions were almost entirely limited to the right lung. There was haemoptysis, which is rare in this disease. Although there was no bronchial growth, there was considerable thickening of the bronchial mucosa suggesting granulomatous infiltration of the mucosa, and apparently the haemoptysis was due to erosion of the diseased mucosa.

Abdominal

Hodgkin's disease in the urinary bladder.—K. Walker reports the case of a man, aged 19, admitted with the diagnosis of Hodgkin's disease, who had great frequency of micturition, dysuria, and on one or two occasions haematuria. Pain was intense and disturbed him 20 to 30 times during the night. Cystoscopic examination under an anaesthetic showed nodules the size of grape seeds scattered over the mucosa of the bladder. A course of deep X-ray therapy gave complete relief, and cystoscopy showed that the bladder had become normal. This appears to be the first case, or one of the first cases, to be diagnosed during life, of Hodgkin's disease involving the urinary bladder. R. Phillips reports the case of a man, aged 32, with Hodgkin's disease in the bladder. Apart from enlarged glands in the neck and axillae, he began to suffer from frequency, acute pain on micturition, and a yellow discharge after passing urine. Cystoscopy showed that the vesical mucosa was studded with greyish-yellow nodules the size of grape seeds, and that there were a few submucosal haemorrhages. After the application of 10 daily doses of 140 roentgens to the bladder, the symptoms subsided, and another cystoscopy showed a normal bladder.

Diagnosis and Differential Diagnosis*Gordon reaction*

Reliability.—P. E. Steiner, employing the Gordon reaction, found that it was positive in 16 (76.2 per cent) of 21 cases of Hodgkin's disease. Of 310 cases previously reported the test was positive in 229 (73.9 per cent). In the author's experience with 40 control lymphatic glands there were no positive reactions, while of 452 control cases collected from publications, positive results were reported in 8 (1.77 per cent). A critical review of these 8 cases showed that in most, if not all, of them the involved tissue could have been differentiated from Hodgkin's disease by histological criteria. The Gordon reaction is therefore reliable in the differential diagnosis of Hodgkin's disease if it is accompanied by histological examination, and the test is very useful in differentiating closely related types of lymphadenopathy. The distribution of the Gordon agent is such as to make it unlikely that it is the causal agent of the disease.

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HYDATID DISEASE

See also B.E.M.P., Vol. VI, p. 538; Cumulative Supplement, Key Nos. 692-701; and Surveys and Abstracts 1939, p. 376.

Cysts of the Kidney*Clinical picture*

Surgical treatment.—W. A. Barrett describes a case of a hydatid cyst of the kidney in a woman aged 23. She had pain in the left flank and left kidney region, some frequency,

nocturia, and occasionally haematuria. She had lost considerable weight. A left nephrectomy was performed, and the lower pole of the kidney was found to be considerably enlarged. On section two cysts were found, each filled with daughter cysts.

Cysts of the Bones

Involvement of ilium

M. Hood, C. N. Lambert, and H. B. Thomas report a case of hydatid cyst of the bone in a woman aged 55. Four months before examination the patient had fallen and injured her left hip. Although the patient had kept a goat and a dog, the extent of the growth indicated that she had acquired the disease as a child in Poland. X-ray of the pelvis showed irregular decalcification involving most of the left ilium and several radiolucent areas suggesting pathological fractures. On operation a cystic cavity was found extending through both tables of the ilium and into the roof of the acetabulum. Here many small cysts were found which were tentatively identified as hydatid cysts. The skin tests with sheep hydatid fluid gave positive results.

Barrett, W. A. (1940) *J. Urol.*, **44**, 389.

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HYDROCEPHALUS

See also B.E.M.P., Vol. VI, p. 566; and Surveys and Abstracts 1940, p. 344.

Aetiology

Unilateral hydrocephalus

R. M. Stewart records 2 cases of unilateral internal hydrocephalus in a female idiot aged 14, and a male idiot aged 19, in whom there was not any obstruction of the interventricular foramen (of Monro), and reviews the subject of unilateral internal hydrocephalus. He collected about 20 previously recorded cases of unilateral internal hydrocephalus, of which 12 appear to have been due to some morbid condition of the cerebral wall which becomes so weakened as to be unable to resist even the normal pressure of the cerebrospinal fluid in the ventricle on the affected side. The 2 recorded cases belong to this non-obstructive group. The cause of the shrinkage and atrophy of the cerebral wall may be encephalitis, meningitis, or vascular obstruction. In the obstructive group of cases the interventricular foramen instead of being so closed as commonly occurs, as to block the opening into both lateral ventricles, does so on one side only. The accounts of the 2 cases are accompanied by 7 illustrations, macroscopic and microscopic.

Stewart, R. M. (1940) *J. ment. Sci.*, **86**, 591.

HYPERCHLORHYDRIA

See also B.E.M.P., Vol. VII, p. 1; Cumulative Supplement, Key No. 708; and Surveys and Abstracts 1939, p. 377.

Aetiology

Effect of fruit juice on gastric function

H. W. Haggard and L. A. Greenberg report the effect of tinned grape-fruit, orange, pineapple, prune, and tomato juice on gastric acidity, peptic activity, and emptying time of the stomach. It was found that, during the early phase of digestion, the pH of the gastric juice may be influenced directly by the acids of the fruit juices, whereas at the height of digestion there was not any appreciable difference in the pH of the gastric juice after meals given with water or fruit juice. The minimal pH was reached with pineapple juice in a shorter time than with the other fruit juices, and the subsequent rise of pH was more marked. Peptic activity in the stomach was not seriously retarded by any of the fruit juices, and was stimulated by pineapple juice. All the fruit juices delayed slightly the emptying time of the stomach after a meal of carbohydrate.

Haggard, H. W., and Greenberg, L. A. (1941) *Amer. J. digest. Dis.*, **8**, 163.

HYPNOTISM

See also B.E.M.P., Vol. VII, p. 34; and Surveys and Abstracts 1939, p. 378.

Methods of Inducing Hypnosis

Evipan

Investigation of neuroses.—E. Stungo found evipan analysis to be a useful and rapid method of investigating cases of suspected neurosis in which no obvious psychogenic factor has been discovered by other methods. If the psychogenesis has become apparent, the hypnotic state induced by evipan is useful for treatment. Synthesis and interpretation may be attempted during the pre-anaesthetic or post-hypnotic phases, depending on the reaction of the patient to the drug. Failure to identify the psychogenic factor by this method tends to rule out a diagnosis of neurotic illness. A single dose of evipan has often restored function in cases of hysterical amnesia and paresis without the aid of psychotherapy. The technique of administration is as follows. The patient is asked to count numbers from 50 in reverse order. Ten cubic centimetres are given intravenously, the solution being injected at about the rate of 1 cubic centimetre per minute, and that rate is maintained until the patient shows some confusion, a point generally reached after 1 to 3 cubic centimetres have been injected.

The injection is then interrupted, the needle being left in the vein. The investigation can then be begun, and the pre-anaesthetic state is maintained by the injection at the same slow rate just enough to maintain that state.

Stungo, E. (1941) *Lancet*, **1**, 507.

HYPOGLYCAEMIA AND HYPERINSULINISM

See also B.E.M.P., Vol. VII, p. 42; Cumulative Supplement, Key No. 712; and Surveys and Abstracts 1939, pp. 72 and 378.

Aetiology

Atrophy of adrenals

Spontaneous hypoglycaemia.—J. G. Rushton, R. W. Cragg, and L. K. Stalker describe the case of a woman, aged 37, suffering from spontaneous hypoglycaemia and paranoid delusions of 7 years' duration. At operation no tumour of the pancreas or any other cause of the attacks could be found. She died shortly after the operation, and necropsy showed extreme atrophy of both adrenals, cortex, and medulla. This was considered to be the cause of the hypoglycaemia. In spite of this extreme atrophy of the adrenals the patient had not shown any of the cardinal signs or symptoms of Addison's disease with the possible exception of low blood pressure and increased sensitivity to insulin. Another finding which might possibly have influenced the metabolic disturbances was the extensive inflammatory destruction of the thyroid, described by Hashimoto.

Rushton, J. G., Cragg, R. W., and Stalker, L. K. (1940) *Arch. intern. Med.*, **66**, 531.

IMMUNITY AND IMMUNIZATION

See also B.E.M.P., Vol. VII, p. 58; Cumulative Supplement, Key Nos. 721–728; and Surveys and Abstracts 1939, p. 379.

Active Immunity

Acquired immunity

Effect of ultra-violet irradiation.—According to A. Eidinow, exposure of the skin to ultra-violet rays diminishes the local reaction normally produced in allergic patients by scarification and the application of hay-pollen toxin. The intradermal injection of hay-pollen toxin into an area of irradiated and erythematous skin of allergic patients excites violent symptoms and signs of hay fever or asthma with collapse. The intradermal injection of T.A.B. vaccine into areas of skin rendered erythematous by ultra-violet rays provokes an agglutinin (H and O groups) titre in the blood serum more than 10 times as great as a similar intradermal injection into areas of normal skin. The erythema reaction after exposure of the skin to ultra-violet rays may thus be used to increase local and general immunity.

Passive Immunity

Analysis of diphtheria antitoxic serum

R. A. Kekwick, B. C. J. G. Knight, M. G. Macfarlane, and B. R. Record describe an analysis of the serum from a diphtheria antitoxic horse by electrophoretic technique showing that both the euglobin and pseudoglobulin fractions of the serum consist of α , β , and γ globulins of which β and γ are antitoxic. Both are specific antibodies in that they neutralize the Park-Williams 8 strain diphtheria toxin in the animal test for potency (L+) and flocculate in a balanced mixture (Lf). β globulin, however, has a higher flocculation time than γ globulin, a lower *in vivo/in vitro* ratio (L+Lf), and the composition of the floccules differ. During the immunization of a horse with diphtheria toxin it was found that the proportion of γ antitoxin to β increased rapidly to a fixed level, but the amount of β antitoxin rises slowly to a higher level, and in the end is in higher proportion. The avidity of antitoxin first precipitated in the salting-out process is known to be greater than later precipitates. As γ antitoxin precipitates at lower salt concentration there may be a connexion between avidity and γ globulin concentration. Serum produced by the pepsin process, although having a short flocculation time, is thought to be a derivative of globulin, judged by the *in vivo/in vitro* ratio. McSweeney's antitoxic serum from early bleeding was thought to conform with γ globulin properties but that from later bleeding had a lower γ component. The importance of considering the β and γ content of antitoxic serum, apart from other properties, is emphasized.

Practical Applications

Diphtheria

Antitoxin level in pregnancy.—J. Liebling, G. P. Youmans, and H. E. Schmitz found that non-immunized Schick-positive mothers did not show any rise in the antitoxin level during pregnancy whereas non-immunized Schick-negative mothers all showed a rise in the antitoxin content during pregnancy. Infants born to Schick-positive mothers were generally Schick-positive, and had an antitoxin content in most cases equal to that of the mothers at term. Infants born to actively immunized mothers gave negative Schick tests, and had an antitoxin level in most cases equal to that of the mothers at term. The maximal antitoxin level in the mothers' blood was reached in a period of 4 to 8 weeks.

Tetanus and diphtheria.—J. A. Bigler and Marie Werner employed combined immunization against tetanus and diphtheria in infants and young children, with successful results. It was found that a stimulating dose of tetanus toxoid given to an immunized child caused a rapid and high response of antitoxin. During 2 years of observation it was found that the period

of immunity to tetanus as measured by the level of antitoxin in the blood serum was as long as that to diphtheria. Two injections of 1 cubic centimetre of the combined toxoids, or 3 injections of 0.5 cubic centimetre produced an adequate basic immunity, and intervals of 3 months or more between injections increased the response of antitoxin. The authors conclude that combined immunization against tetanus and diphtheria seems to be as practical as immunization against diphtheria alone.

Streptococcal infections

Reliability of Dick test.—H. A. Reisman and A. Berkow discuss the discrepancies in the results of the Dick test for scarlet fever. There is no doubt as to the specificity of the haemolytic streptococcus used in pure culture in the Dick test. Observations were made on two groups of scarlet fever patients who were subjected to the Dick test on admission to hospital, the day of illness being usually the third or fourth. The toxin for group 1 was prepared in meat broth and for group 2 contained peptone, or proteose and dextrose, but no protein. Both groups were inoculated with Dochez N.Y. pure strain incubated and standardized as to potency; the group 2 toxin showed higher potency and minimized urticarial reactions. Approximately 1 cubic centimetre was injected intracutaneously and reactions noted after 18–24 hours. The test was repeated after 12 days and 19 days. Reddening up to 10 millimetres was taken as a positive reaction. Results showed that in group (1) 37 per cent of the positive cases became negative after 12 days, and 54 per cent after 19 days. In group (2) 89.7 per cent positive cases became negative after 12 days and 88 per cent after 19 days. This change indicates the development of immunity. Reversal from negative to positive in group (1) occurred in 3 per cent of cases after 12 days and in 15 per cent after 19 days, and in group (2) in 9 per cent of cases after 12 days and in 5.7 per cent after 19 days. This is too frequent to be accidental. Similar discrepancies have been found by others. It is difficult to explain these and the differences between the two groups which cannot definitely be attributed to different reactions to bacterial nucleoprotein. The Dick toxin, which is a pool of 4 selected strains, produces an antitoxin which is known to have failed in 10 per cent of cases to neutralize toxin strains from fever patients. The authors used a single pure strain. This may partly explain the discrepancy. The production of throat infection without rash is noted even in cases giving negative Dick tests, indicating immunity from erythrogenic but not from angina. The Schultz-Charlton test was also applied to the two groups and agreement with the Dick test was noted in 69 per cent in group 1 and 45 per cent of cases in group (2).

Enteric fevers

T.A.B.C. vaccine.—A. Felix, S. G. Rainsford, and E. Joan Stokes report on a new T.A.B.C. vaccine, killed and preserved with alcohol, and compare it with ordinary heat-killed T.A.B. or T.A.B.C. vaccine. There are two marked differences between groups of subjects inoculated with these vaccines. The alcohol-killed and preserved vaccines stimulated demonstrable typhoid Vi antibodies in a relatively high proportion of cases, whereas the Vi antibody response to ordinary vaccines was almost negligible. No significant difference in O antibody response was noted. The reactions produced by the new vaccine were much milder; general reactions were as a rule either absent or quite trivial, and the local reaction was of a modified type.

Bigler, J. A., and Werner, Marie (1941) *J. Amer. med. Ass.*, **116**, 2355.

Eidinow, A. (1941) *Lancet*, **1**, 540.

Felix, A., Rainsford, S. G., and Stokes, E. Joan (1941) *Brit. med. J.*, **1**, 435.

Kekwick, R. A., Knight, B. C. J. G., Macfarlane, M. G., and Record, B. R. (1941) *Lancet*, **1**, 571.

Liebling, J., Youmans, G. P., and Schmitz, H. E. (1941) *Amer. J. Obstet. Gynec.*, **41**, 641.

Reisman, H. A., and Berkow, A. (1941) *Arch. Pediat.*, **58**, 286.

IMPOTENCE

See also B.E.M.P., Vol. VII, p. 103; Cumulative Supplement, Key No. 736.

Treatment

Drugs

Testosterone propionate.—A. W. Spence employed testosterone propionate in doses varying from 50 to 100 milligrams intramuscularly, 3 times a week for 2 to 6 weeks, in 6 cases of functional impotence unassociated with any evidence of testicular dysfunction. In no case was there any sign of improvement. Since these doses are sufficient to cause prolonged erections in eunuchs, the author concludes that testosterone has no effect on impotence due to psychological disturbances.

C. D. Creevy and C. E. Rea employed testosterone propionate in 12 cases of impotence. Although the patients felt better psychically after the treatment, there was not any improvement as regards impotence. Similar results were obtained when sesame oil was injected into 3 patients. The authors conclude that the benefits of the drug in cases of impotence without hypogonadism are chiefly psychical.

Creevy, C. D., and Rea, C. E. (1940) *Endocrinology*, **27**, 392.

Spence, A. W. (1940) *Brit. med. J.*, **2**, 411.

INFANT FEEDING: THE FEEDING OF NORMAL INFANTS AND CHILDREN

See also B.E.M.P., Vol. VII, p. 136; Cumulative Supplement, Key Nos. 749–753; and Surveys and Abstracts 1939, p. 381; 1940, p. 346.

Breast Feeding*Relation of maternal diet to lactation*

Effect of cystine, glycine, and glutamic acid.—R. G. Daggs gave 1 gramme each of cystine, glycine, and glutamic acid before breakfast, 2 grammes of each with dinner, and 2 grammes of each with supper to 4 multiparae all of whom had a history of either failing or no milk supply with previous babies. These amino-acids were either sprinkled on the food or given in lemonade. In all cases the milk secretion was stimulated; analysis of the milk in 1 case showed an increased fat-content after cystine feeding.

Excretion of mandelic acid.—H. Berger states that mandelic acid is excreted in breast milk in quantities somewhat less than those of the normal daily dose of this drug, i.e. 0.18 gramme per kilogram of body weight. Thus babies of nursing mothers who are being given mandelic acid in normal dosage under ideal conditions of administration never receive a dangerous amount of the drug. No clinical or laboratory evidence of damage to the nurslings of these mothers was found.

Inhibition of lactation

Stilboestrol.—C. W. Mucklé employed stilboestrol in 75 puerperal women to inhibit or suppress lactation. The dosage was 5 milligrams 3 times a day, for a total of 6 doses; this relieved engorgement of the breast, and decreased or prevented lactation in all cases. In 40 per cent of 53 patients observed there was a secondary occurrence of lactation. This was generally painless and slight in amount. Only 2 patients were nauseated.

Wet-Nursing and Feeding with Artificial Foods up to Age of 9 Months*Use of dextrin-maltose-dextrose carbohydrate*

G. N. Krost found that the results obtained by feeding new-born infants with a liquid dextrin-maltose-dextrose carbohydrate mixture compared favourably with those obtained by dextri-maltose. To 100 new-born infants a 5 per cent dextrin-maltose-dextrose solution was given 6 and 12 hours after birth, and every 4 hours thereafter, as pre-lacteal feeding. If complementary feeding was required, evaporated milk 1 part, water 2 parts, and 5 per cent added carbohydrate were given. A control group of 100 babies was given a 5 per cent dextri-maltose solution. There was a slightly smaller initial weight loss and greater increase in weight on discharge in the group fed on the liquid dextrin-maltose-dextrose mixture, and there were fewer stools. The author concludes that this mixture is a perfectly safe form of carbohydrate.

Feeding of Older Children*Banana intake*

H. A. Hunscher, F. C. Hummel, and I. G. Macy studied the influence of different levels of banana intake on the nitrogen and mineral balances of 8 normal children 5 to 8 years of age. They found a definite consistent metabolic response to an increased banana intake. Ingestion of an additional 100 grammes of banana daily was accompanied by increased retention or an increased percentage of intake retained of nitrogen, calcium, magnesium, sodium, potassium, phosphorus, chlorine, and sulphur. The investigation showed the benefit due to inclusion of banana in the diets of normal children.

Berger, H. (1941) *Amer. J. Dis. Child.*, **61**, 256.

Daggs, R. G. (1940) *Amer. J. Obstet. Gynec.*, **40**, 457.

Hunscher, H. A., Hummel, F. C., and Macy, I. G. (1940) *Amer. J. Dis. Child.*, **60**, 509.

Krost, G. N. (1941) *Arch. Pediat.*, **58**, 243.

Mucklé, C. W. (1940) *Amer. J. Obstet. Gynec.*, **40**, 133.

INFLUENZA

See also B.E.M.P., Vol. VII, p. 173; Cumulative Supplement, Key No. 754; Surveys and Abstracts 1939, p. 383; and p. 3 of this volume.

Aetiology*Epidemiology*

Variation of virus strains.—Writing on the fundamental problem of the explanation of the numerous recurrences of epidemic influenza, T. Francis, Jun., while not neglecting the pioneer work of W. Smith, C. H. Andrewes, and P. P. Laidlaw (1933) and others, draws largely on the evidence with which he has been personally connected from 1935 to 1940. The frequency of the occurrences in adult populations indicates that epidemic influenza differs immunologically from many of the common infections and that either immunity is short-lived, or that serologically divergent strains of virus are disseminated in different outbreaks and that the strains vary in virulence and infectivity. From 1933 to 1936 various laboratories were occupied in the isolation of the virus in epidemic areas and the establishment by immunological means of the identity of the virus involved; since January 1936, 4 epidemics have been investigated and yielded some interesting contrasts. Immunological and epidemiological observations point to the existence of 2 influenzas, A and B, with different virus strains and different clinical features, mild or severe. The 2 large outbreaks of influenza B in 1936

and 1940 began in the early months of the year, whereas the tendency of the 4 epidemics of influenza A in alternate years since 1932–3 has been to gain momentum in November or December. It might therefore be suggested that influenza A recurs biennially and influenza B quadrennially.

National health in war-time.—At the end of March, W. Jameson, Chief Medical Officer of the Ministry of Health, stated that 1941 would not be regarded as an epidemic year for influenza. The peak period for influenza and for cerebrospinal fever, the mortality from which in 1940 had been highest on record in Great Britain, had now passed. It was unlikely that there would be a high toll from these diseases this year. Among the reasons for the fortunate conditions ruling during this last epidemic season were the more dispersed state of the population, diminished travelling, fewer attendances at cinemas, more simple food, and the fall in the number of those out of work, since useful occupation inhibits excessive self-concern.

Clinical Picture

Acute bronchiolitis

D. Hubble and G. R. Osborn claim that acute bronchiolitis is the essential pulmonary lesion in epidemic influenza. The condition is particularly common in young children, in whom it produces urgent dyspnoea and, unless prompt and careful treatment is given, death by asphyxia. The authors suggest that the respiratory obstruction is caused by mucus in the bronchioles. Essential therapeutic measures consist in the use of sulphapyridine, steam, and oxygen. In the hands of an expert, bronchoscopic aspiration may be life-saving.

Buccal spots

E. Wolff observed, after the toothless period of infancy, characteristic changes in the buccal mucosa of patients with influenza and common colds. These changes, which the author calls buccal spots, appear to be pathognomonic of these infections. The spots are believed to be due to trauma by the teeth of a mucosa which has become vulnerable in the course of the infection. They always appear in the area of the bite line. In order to observe them the whole mouth must be examined in a good light. The spots are essentially different from the lesions of traumatic injury, of aphthous stomatitis and from Koplik's spots. They appear within the first 3 days of illness and persist for several weeks. They are entirely painless.

Francis, T., Jun. (1941) *Trans. Studies, Coll. Phys., Phila.*, 4 ser., 8, 216.

Hubble, D., and Osborn, G. R. (1941) *Brit. med. J.*, 1, 107.

Jameson, W. (1941) *Med. Offr.*, 65, 113.

Smith, W., Andrewes, C. H., and Laidlaw, P. P. (1933) *Lancet*, 2, 66.

Wolff, E. (1941) *Arch. Pediat.*, 58, 1.

INJURIES

See also Surveys and Abstracts 1939, p. 383; 1940, p. 347; and pp. 8, 9, and 92 of this volume.

Wounds

Clinical picture

Serum protein concentration.—H. Koster and A. Shapiro estimated the concentrations of total protein, albumin, and globulin and calculated the oncometric pressure of serum in 58 cases of operative wounds. Patients with deep infection or disruption of wounds showed lower values for total protein and for oncotic pressure in their serum. This was due mainly to a diminution of the albumin fraction. The occurrence of normal concentrations of serum protein and albumin in some patients with infected or disrupted wounds, and the relatively low concentrations in some with clean wounds, implies that hypoproteinaemia by itself is neither a necessary nor a sufficient condition for the development of wound infection or disruption.

Rupture of liver with subsequent 'sequestrum'.—R. Clarke describes a case of a rare lesion: a liver 'sequestrum' complicating a subcutaneous rupture of the liver. The patient, a youth of 18, had an extensively ruptured liver after being run over by a lorry wheel across the abdomen. Most of the tear was closed with deep mattress sutures of stout catgut which included the falciform ligament. One part was packed with gauze. The total loss of blood was calculated to be 2.4 litres out of a total of 4 litres, but it was replaced by blood and serum transfusions. After an uneventful post-operative course, the temperature rose and there was abdominal tenderness with copious discharge from a small unhealed sinus. Lipiodol was injected and a radiological examination showed a cavity continuous with a tributary of the bile-duct. On further examination the cavity contained a detached liver 'sequestrum' which was necrotic but not autolysed liver tissue. Its removal was followed by recovery.

Surgery

Tulle gras dressings.—According to D. N. Matthews, the ideal treatment for all raw surfaces is *tulle gras*, which consists of close-meshed curtain net cut into squares of suitable size and impregnated with soft paraffin 98 parts, balsam of Peru 1 part, and olive oil or other vegetable oil 1 part. The net is cut to fit a tin box some 5 inches square and 2 inches deep and is packed in layers, each piece of net being separated by a sheet of white paper to facilitate its removal. The paraffin mixture (250 grammes for a tin of these dimensions) is added, and the tin is sterilized by heat for an hour at 150° C., after which it is sealed with adhesive tape. An

analgesic effect is obtained by the addition of 1 per cent powdered decicain base, or 0.1 per cent of powdered percaine base. If the surface to be covered is sterile, as in the area made by cutting a Thiersch graft, the *tulle gras* is left for 10 days, covered with gauze and a bandage, when the skin will be found to have healed painlessly. For infected wounds and burns saline packs, sulphanilamide powder or other dressing can be applied daily or hourly without causing any pain, as the *tulle gras* is left in situ until it should be renewed because of the loss of the paraffin base and its contained anaesthetic. This form of dressing has the additional advantage that, owing to the open mesh of the net, there is not any risk of damming back the discharge, which escapes freely into the overlying gauze.

Petroleum jelly dressings.—O. Tenopir and F. M. A. Akl claim that the ideal dressing for clean post-operative wounds is one of petroleum jelly spread over the wound, and covered with a film of cellulose, then with dry gauze pads. This dressing promotes oozing from the wound by its anti-coagulant anti-evaporating properties. It seals the wound to accidental spilling of infected material and prevents contamination with infected gases. It facilitates inspection of the wound whenever infection is suspected, and relieves pain and saves time when the dressing is changed. Growing epithelium and fresh granulations are not disturbed when the dressing is removed.

Amnioplastin.—L. Rogers employed amnioplastin in the surgery of 8 intracranial and 12 peripheral nerve cases, and in several other lesions, such as a scar in the popliteal space. Except in 1 intracranial case, that of a large recurrent meningioma, all wounds healed by first intention. Early functional restoration was noted in most, and freedom from pain in all cases. In the peripheral nerve cases, after the nerve trunk had been isolated and freed from both above and below the level of the lesion, the site of the lesion was wrapped in a suitably shaped piece of amnioplastin. The results were encouraging, relief from pain and restoration of function following its use.

W. Penfield publishes a warning against the use of amnioplastin, prepared from human amniotic membrane, for the prevention of adhesions between the dura mater and the lacerated brain, when the substance is improperly prepared. In a previous communication on the experimental use of the amnioplastin Y. Chao, S. Humphreys, and W. Penfield described the method of preparation, and recommended either soaking in alcohol followed by boiling in distilled water for 20 minutes or, alternatively, dry sterilization in an autoclave. The authors now report an unsatisfactory result in a patient with membrane prepared by the latter method. It is now evident that if the membrane is to be used in man, boiling should not be omitted.

Skin grafting.—C. Szutu and C. Y. Chen maintain that, to obtain the best results in skin grafting, there must be good approximation of the opposing surfaces, these surfaces must be adequately immobilized, and provision for the free escape of serum must be made. They describe a simple method of immobilizing Thiersch grafts. The surrounding skin is carefully sponged dry and freed from grease with ether. A single layer of gauze is stretched over the graft and trimmed so that its margins extend over the normal skin for a distance of about 2 centimetres. This is anchored to the skin by the application of flexible collodion. The collodion must not be allowed to run into the wound. Before the collodion dries, the gauze is pressed further on to the surface of the wound by means of a large gauze sponge moistened with normal saline solution. Over the first layer of gauze are placed many layers of dry gauze which have been trimmed to accord with the size and shape of the grafted area. The whole dressing is pressed and anchored in position by short narrow strips of flamed adhesive plaster. The wound can be inspected by lifting the layers of gauze, leaving the first layer undisturbed. This method gave good results.

Soluble rod method of vascular anastomosis.—S. Smith describes a new method of simplifying vascular anastomosis by means of a soluble rod introduced into the vessel to supply mechanical form and support during the suturing process. The soluble rod, composed of dextrose, dissolves in less than a minute in the blood stream after the circulation is restored. Histological examination did not show any evidence that the use of the dextrose rod damaged the vessel walls.

Synthetic plastic sutures.—J. E. Bellas maintains that the ideal suture must be one that is non-reacting, not affected by enzymatic, chemical, physiological, bacteriological, and physical influences and one which assists prompt, normal repair. Catgut, silk, and sutures of animal origin are of protein composition and as such, act as reacting foreign bodies, more or less intensively. They are also subject to numerous chemico-physiological, bacteriological, and physical influences, the total effect of which is to hinder and delay primary repair in operative wounds. The author employed a new suture composed of synthetic plastic materials consisting of polymerized condensation products of aliphatic and aromatic alcohols with aliphatic aldehydes. No intraperitoneal complications have arisen from the use of this as continuous sutures in the peritoneal cavity in either clean or infected cases. This new suture material appears to approach the ideals mentioned above.

Coagulated blood plasma in nerve suture.—J. Z. Young and P. B. Medawar, endeavouring to reduce the difficulties of nerve suture and to minimize the disorganization of the fibres which is apt to be produced by stitches, even if restricted as far as possible to the epineurium, devised a method by which stumps can be held together with concentrated coagulated blood plasma. The method consists in holding together the cut stumps, and pouring round them plasma which has been mixed with a little tissue extract (fibrinogen to increase the normal

fibrinogen content up to as much as tenfold). In about $\frac{1}{2}$ to 2 minutes, according to the age of the plasma and the strength of the extract, the plasma clots into a firm jelly which sticks to the nerves and holds the stumps together. The plasma is freely permeable, and during the subsequent days is dissolved, although it remains long enough to allow a firm union to be established between the divided ends. The authors found that the cut sciatic nerve of the rabbit and dog could be effectively joined by this method. New fibres grow slightly faster across such a junction than across a sutured nerve, and good funicular apposition is secured. The distance of outgrowth of axons in the peripheral stump can be determined by pinching the nerve to discover the most peripheral point from which reflex responses can be obtained. It thus shows that in the rabbit, after plasma junction, the fibres grow through the peripheral stump at the rate of 3.9 millimetres a day, after a latent period of 8.1 days.

'Windowed' unpadded plaster of Paris casts.—H. D. Cogswell and C. A. Thomas describe a method of protecting the skin in 'windowed' unpadded plaster of Paris casts. The unpadded plaster of Paris splint is applied in the usual manner, and the area to be removed is outlined by an indelible pencil. A window of the proper size is cut, bevelling the edges of the cast so that the smallest diameter is on the inner side next to the skin. The bevelled edges of the cast are then lined with adhesive tape, and the wound covered with 5 or 6 thicknesses of gauze. A strip of wet plaster gauze is wadded and packed into the opening and pressure applied until it hardens. The plug may be varnished to prevent its softening by drainage. The tape lining and bevelled edges make the plug easy to remove, and it is held in position by a bandage which envelops this portion of the cast.

Injuries of tendons.—N. J. Howard states that trauma to the tendon-traction apparatus must involve the vascular structures to render possible a response towards healing. The attempt at healing may produce clinico-pathological phenomena arising from interference with free unimpeded tendon motion, or from vascular erosion of tendon fibres. Thus a single tendon injury, or repeated tendon injuries, may cause diseased states which may become chronic, or may appear to be unrelated to the initial injury.

M. L. Mason and H. S. Allen state that the holding power of tendon for the suture shows a marked drop below its original power and does not begin to rise until the fifth day after suture. It does not rise consistently above the strength of the sutures until the fourteenth day. The importance of adequate relaxation during this time is evident.

Surgery of air-raid casualties

D. N. Matthews reviews the experiences gained in the surgery of air-raid casualties. For a hospital reception centre for more than 50 patients a staff of 2 resident surgeons, 2 anaesthetists, radiographer, house surgeon, reception officer, blood transfusion team, post-mortem attendant with assistants, and a strong team of stretcher-bearers is recommended. The surgery of minor wounds before transfer of the casualty to the base is suggested. For the treatment of shock, transfusions of plasma or dried serum proteins are best, but whole blood should be used in cases of severe haemorrhage. Stored blood and plasma must be filtered before use. Preliminary X-ray examinations are essential before surgical measures are adopted. Brick dust must be washed and scraped from the epidermis. Each glass wound should be examined for fragments, but débridement of the edges is unnecessary. Immediate suture and the spraying of open wounds with sulphanilamide powder before closure have given good results. All raw surfaces are now sprayed with doses higher than the suggested maximum of 15 grammes with no ill effects. Compound fractures are approached with large incisions to remove lacerated muscles, and amputations are rarely performed. Plaster encasements are used, cut from end to end with a window over the wound, which is sprayed daily with sulphanilamide powder and covered with dry gauze. Sulphathiazole is added to remove staphylococci and contaminants. The plaster is then closed. Large incisions are made in cases of gas gangrene and all muscle tissue removed. Sulphanilamide powder is sprayed and the wound lightly packed with dry gauze. The plaster is wedged open to allow for swelling. Anti-gas gangrene serum (40 cubic centimetres) is given intramuscularly and sulphanilamide (30 grains) by mouth daily. Gas organisms were not recovered after 48 hours. Nerve palsy due to crushing without wounding has been slowly cured without operation. Small steel fragments may be left, but large fragments in the muscles or near the joints must be removed. Antitetanic serum is always given (3,000 units), and there have not been any cases of tetanus. Tannic acid sprays or tannafax jelly are applied to shallow burns, but when the skin is destroyed daily immersion in saline baths of increasing concentration is suggested, followed by dressings of *tulle gras* (vaseline-impregnated net) sprayed with sulphanilamide powder and overlaid with saline moistened gauze. Grafting can be started when the haemolytic streptococci have disappeared.

Infection

Chemotherapy.—A discussion at the Royal Society of Medicine on chemotherapy and wound infection was opened by the late Sir W. Willcox, President of the Section of Therapeutics and Pharmacology, who reviewed the progress of sulphanilamide therapy. L. Colebrook described sulphanilamide as a diffusible, readily absorbed, innocuous, easily soluble substance with a low affinity for body proteins. Its action on leucocytes was not known; a solution of 1 in 400 of sulphanilamide had not any harmful effect on leucocytes. It had been used successfully as an antiseptic powder in compound fracture wounds. It lessened the danger of gas gangrene and streptococcal infection. An occlusive dressing with sulphanilamide was needed to prevent infection and fluid loss in burns. E. E. Lewis described the successful

local use of sulphanilamide powder (using streptocide, Evans, Sons, Lescher, and Webb) in addition to M & B 693 orally, in (1) cases of wounds with gas gangrene, and (2) in the treatment of burns after other unsuccessful treatment. The burns were washed in soap and water, the loose skin removed, 70 per cent spirit applied, then the streptocide powder put on and covered with *tulle gras*. The depth of the wound was obliterated (after powdering) with catgut sutures, and anti-gas serum was not used. R. Mowlem reported on the successful use of sulphonamide preceding skin grafts. In spite of the high rate of infection there was only 1 failure out of about 40 cases, compared with a success rate of 18 per cent (complete) and 27 per cent (partial) with previous treatments. Sulphonamide was massaged into the wound making a paste of the serum. Two grammes of sulphonamide were given by the mouth before the operation and 5 cubic centimetres of soluseptasine on the operating table. A. Fleming described *in vitro* experiments to show that the so-called specificity of sulphanilamide, sulphapyridine, and sulphathiazole was due to their different potencies. Sulphathiazole was more potent than sulphapyridine against staphylococcus and other bacteria commonly found in war wounds. They were both more potent than sulphanilamide, which was only effective against *Streptococcus pyogenes*, but which was more readily absorbed than the other two. The sulphonamides only affected leucocytes in very high concentrations, but they were inhibited by pus and large numbers of bacteria. Penicillin had been extracted in impure form from penicillium and was 20 times as potent as sulphathiazole against staphylococcal and streptococcal infections. It was not inhibited by pus and bacteria. Similar extracts from other organisms had been obtained. Sulphonamide treatment should be accompanied by immunization, which may be a deciding factor in its success. F. Hawking recommended a mixture of sulphanilamide and sulphathiazole which had been proved to be as effective as the latter alone against *Cl. welchii* and *Cl. septique*. It should be reinforced by prophylactic injections of antitoxin and applied as soon as possible locally rather than orally. No inhibiting action by pus had been found. C. A. Green could not find any evidence in his experiments for interference by prontosil with antibody production, nor antistreptolysin O production, and neither prontosil II nor its derivatives had a neutralizing effect on streptolysin O. A. E. Francis reported success in the treatment of superficial wounds with local insufflation of sulphanilamide powder, which should be applied directly to the wound and kept moist. Streptococci occurred round the wound and should be cleaned off. There were many cases of secondary infection late in the treatment, often of different strains. For a more delicate test for streptococcus before grafting, blood-agar plates containing 1:500,000 gentian violet were used. K. Wallersteiner pointed out the low toxicity of sulphanyl flavine to fibroblasts and epithelium and its solubility in glycerol. Various derivatives of -I-amino-8-naphthol-3:6 disulphonic acid stimulated fibroblasts and combined with an active antiseptic should give good results.

Early precautions.—H. S. Allen recommends the management of an open wound, superficial or deep, by the application of a simple sterile dressing immediately after injury to prevent further contamination and to control haemorrhage. Thereafter every effort should be made to maintain strict asepsis and to prevent secondary contamination from human sources. If seen immediately after the injury a wound can be cleansed mechanically with soap and water and converted into a clean wound. An injury seen within 6 or 8 hours can be closed by suture or skin grafting. All wounds may be safely left undisturbed post-operatively until healing has progressed.

Silk sutures in infected wounds.—E. C. Cutler and J. E. Dunphy found that silk can be used in infected wounds without the disastrous results often attributed to it. Advantages of its use are that there is less inflammatory reaction than with other sutures and the degree of infection in the immediate post-operative course is less. Silk sutures are also stronger. In the presence of infection catgut is often rapidly absorbed, whereas silk continues to hold the tissues together. Even when healing has been completed the extrusion of silk sutures may continue.

Local sulphonamide therapy.—W. E. Herrell and A. E. Brown state that the local use of sulphonamides, in certain cases, exerts a definite beneficial effect on the course of infected wounds. They employed a thick suspension consisting of 30 grains of powdered sulphanilamide in 100 cubic centimetres of an 0.8 per cent solution of sulphanilamide in physiological saline solution. It appeared that the suspension was more effective in the prevention of infection than in the treatment of an already well-established infection. Twenty-one cases were treated, including badly infected scalp wounds, surgical or traumatic wounds of the thorax and pericardium, abdominal incisions which did not heal well, and various types of orthopaedic wounds, including fractures, and infected sinuses of soft tissues.

J. A. Key, C. J. Frankel, and T. H. Burford in a discussion of the local use of sulphanilamide, maintain that it should be sterilized before it is placed in clean wounds. They found that the drug was well tolerated in joint and other tissues. The powder slightly inhibits the primary healing of the wound, but not to such a degree as to contra-indicate its use in clean operative wounds. It may be used repeatedly in open infected wounds, and does not seriously interfere with the healing of such wounds. The authors advocate the local use of the drug in both contaminated and clinically clean operative wounds in which infection may be feared, or in which it would be particularly undesirable.

A. C. King treated a number of wounded patients by packing the wounds with sulphanilamide powder. Sulphanilamide was not given by mouth and pre-operative treatment was given in ordinary surgical procedures. The skin edges of the wound were excised and the

depth of the wound examined. All fragments of muscle and damaged muscle were removed and all bleeding points ligatured. The powdered drug was then packed into the cavity. The wound was left open and covered with gauze smeared with sterile vaseline, and then with elastoplast, cotton-wool, and bandages. After 5 days the wound was dressed, and delayed primary suture was undertaken. By this time all the sulphanilamide had dissolved, the wound was clean and had begun to granulate, and was suitable for suture.

C. W. Mayo and J. M. Miller report on the use of a solution of sulphanilamide in the local treatment of wounds. They have chiefly employed this solution for the irrigation of wounds after posterior resection or combined abdomino-perineal resection for carcinoma of the rectum. The solution was prepared by heating a physiological solution of sodium chloride to boiling point and adding sufficient sulphanilamide to make a saturated solution (0·8 per cent is the limit of solubility). Irrigations were begun after the posterior pack, inserted at the time of operation, had been removed. Flushing the cavity with hydrogen peroxide solution before irrigation with the solution of sulphanilamide was found to be a useful additional measure. Irrigations were carried out three times daily. After this treatment the wounds became much cleaner in appearance, and granulation tissue was in a healthy state. The authors believe that sulphanilamide stimulated to some extent the growth of connective tissue. The method proved effective in cases in which other drugs had failed.

In view of the danger of the destruction or absorption, as a result of secondary infection, of cartilage implants for the repair of facial defects, J. H. Childrey employed sulphamethylthiazole locally with good results. At the time of operation 7–10 grains of the powdered drug were placed in the wound with the cartilage. As an added precaution the drug was also given by mouth, in a dosage of 45 to 67½ grains daily, for a week or 10 days.

L. Colebrook and A. E. Francis investigated the effect of the local application of sulphanilamide powder to 62 cases of superficial wounds infected with haemolytic streptococci. In 3 patients with 10 wounds the drug was also given by mouth. Haemolytic streptococci usually disappeared from the wounds within 3 or 4 days, and did not reappear. Infections with haemolytic streptococci, group D, proved resistant to local treatment. Neither sulphanilamide nor sulphathiazole had consistent effects on staphylococci, *Bacillus proteus* or *Pseudomonas pyocyanea*, which were also present in the wounds.

Zinc peroxide.—J. A. Gius confirms the value of zinc peroxide in surgical infections. The drug is employed in the form of a suspension in sterile distilled water mixed to the consistency of a 40 per cent cream. The wound into which the suspension has to be introduced must be mechanically cleaned of dead tissue, debris, and exudate; extensions of the wound must be laid open in order that the mixture may reach all recesses. The wound is flooded with the suspension, then gauze saturated with the suspension is loosely packed into it, and the entire area sealed off with either several layers of vaseline gauze or zinc oxide gauze. The dressing is left in place for 24 hours, then removed and irrigated with sterile water. The dressing is repeated until the smears and cultures become negative. In conjunction with zinc peroxide locally, one of the sulphonamide compounds may be used.

Bacteriology of wounds treated by the closed plaster method.—Jean Orr-Ewing, J. C. Scott, and A. D. Gardner report the result of 73 complete analyses of the bacterial flora of 10 cases often with two wounds and all but one of compound fractures, treated by the closed-plaster method. Various types of window were tried, and a satisfactory apparatus, which was embedded in the plaster, was devised for securing bacteriological samples from wounds encased in plaster without interference with the treatment. First, if possible, a sample was taken at the time of excision, and then at short intervals after the application of the plaster. In the later stages examinations were made when the plasters were changed, and usually at less frequent intervals between the changes. Direct microscopical observations of the discharges were made at every examination and served both as a check on the cultural method and as a rough estimate of the absolute and the relative richness of the flora. Haemolytic streptococci belonging to group A and *Staphylococcus aureus* were each found in 7 out of the 10 cases, 5 of them harbouring both cocci. *Clostridium welchii* (Type A toxin) was present for a time in 1 patient who never showed any evidence of gas gangrene. Tables are given of persistent and of non-persistent micro-organisms isolated from the individual patients. Since wholly harmless microbes usually disappear within a few days or weeks, it is remarkable how persistent is the diphtheroid 'Type I'; this contrasts with all the other diphtheroids which disappear in a few days. In normal circumstances infections do not take place through the plaster casing but infection was found to occur fairly often during the application of plaster. The authors' observations do not throw light on the sources of pre-hospital infection—i.e. whether at the time of the accident or by first-aid treatment, as suggested by R. Hare, but it may well occur at this period, in spite of the fact that microbes were often not detected in the wounds for 7 or even occasionally for 15 days after admission. In other words, there seems to be a very considerable lag in the development of many species in wounds which have been thoroughly excised and cleansed within a few hours of the accident. Special attention was paid to the presence in 4 cases of *Pseudomonas pyocyanea*, because it has been suggested that it may exert a favourable influence on wounds and in particular that it may inhibit the growth of *Streptococcus pyocyanea* and *Staphylococcus aureus*. The authors do not find any evidence in favour of this hypothesis. Neither the general composition of the wound flora under closed plasters nor the changes of its composition in the early or later stages have clearly

explained the virtue of the closed-plaster method of treatment; there is not any striking difference in the flora of the 10 cases and of open wounds. There was not in the cases so systematically examined any disappearance or diminution of pathogenic bacteria under the influence of saprophytic anaerobes or of relatively harmless aerobic rods, such as *Proteus* or *Pseudomonas pyocyanea*. Although it cannot be stated that *Streptococcus pyogenes* (group A) is completely innocuous in properly immobilized and protected wounds, it is quite clear that this microbe may be present from first to last in wounds which, under these conditions, heal without obvious complications or gross delay; the same is true of *Staphylococcus aureus*. It is concluded that the efficacy of the closed-plaster method is due to its physical and physiological effects rather than to any specific influence on the bacterial flora.

Hypertonic sodium sulphate and acriflavine solution.—C. J. Cellan-Jones confirms the claims of Lyth regarding the value of hypertonic solutions of sodium sulphate in infected wounds. He, however, recommends a modification of J. C. Lyth's method, combining acriflavine with the sodium sulphate solution. By dissolving a measured quantity of a powder consisting of sodium sulphate and acriflavine in warm water, a 10 per cent sodium sulphate solution containing 0.1 per cent acriflavine can be prepared. The use of this mixture enables spreading infections to be quickly localized, causes more rapid separation of sloughs, and stimulates granulation and epithelial growth to a much greater extent than sodium sulphate alone.

Healing

Cystine hydrochloride.—J. F. Riley maintains that, although migration of cells alone is sufficient for the healing of small wounds, larger lesions require the additional factor of growth by mitosis. Epithelial growth is probably inhibited by fibroblastic proliferation, but, pending further knowledge, deliberate cellular inhibition for long periods may be dangerous as regards tumour formation. Physiological stimulation, on the other hand, would appear to be free from such dangers. There is much evidence to show that compounds of the sulphhydryl ($-SH$) group tend to stimulate growth by mitosis. The author's experiments on rabbits showed that cystine hydrochloride, as an 0.5 per cent ointment in lanolin, gave a 30 to 40 per cent acceleration of healing, by measurement of surface area, in large excised wounds, and a somewhat slower rate of healing in wounds caused by heat. The ointment was tried clinically on the skin reactions after deep X-ray or radium therapy and undoubtedly hastened healing. Employed for a wound which was already granulating, the ointment was not painful. If the patient complained of pain, the cystine could be made up fresh as a 0.5 per cent solution in buffered alkaline phosphate or according to the method of Brunsting and Simonsen. Bed-sores, burns, scalds, and traumatic epithelial defects also responded favourably to the ointment.

Relation to vitamin C and serum protein.—J. B. Hartzell, J. M. Winfield, and J. L. Irvin emphasize the importance of the relation of low vitamin C and low serum protein to poor healing of wounds. Among 1,458 collected cases of wound disruption, 320 (22 per cent) were the subjects of carcinoma and 195 (13.4 per cent) of peptic ulcers. In such cases the nutritional condition of the patient, as shown by serum protein and vitamin levels, is likely to be poor because of restricted diets and, in the case of serum protein concentrations, because of decreased production of proteolytic enzymes.

Mechanism of haemostasis.—In a full critical review of the mechanism of haemostasis which includes numerous personal observations on the power of contraction of capillaries in response to injury in normal persons and in subjects of haemorrhagic diatheses, R. G. Macfarlane reaches the following conclusions: (1) the platelets, apart from their action as accelerators of blood-coagulation and clot retraction, do not appear to be important in the haemostatic mechanism; (2) coagulation of blood alone is incapable of arresting bleeding even from a needle puncture; but the formation of a firm blood-clot is necessary for the maintenance of haemostasis produced by some other factor; (3) capillaries, in certain areas examined, normally contract after injury but this does not occur in the haemorrhagic states associated with the prolonged bleeding time. A tentative hypothesis of haemostasis is formulated: (1) the first normal reaction to injury is haemorrhage from damaged vessels, which are dilated by the action of 'H' substance produced by the trauma; (2) when the 'H' substance has been removed by the flow of blood, or by diffusion, the injured vessels contract and bleeding ceases, the action of the vessels being assisted possibly by agglutinated platelets, though this factor is not essential to haemostasis; (3) during the period of capillary contraction the blood which initially escaped has time to coagulate firmly in the wound and the clot to retract and become securely attached; (4) in normal subjects after the period of contraction, dilatation of the injured capillaries occurs, haemorrhage in open wounds being prevented by the preformed blood-clot; (5) in small punctured wounds the approximation of the edges and the drying of the exudate are enough to prevent the onset of bleeding, and clotting of blood is not necessary. Failure of this mechanism may be due to loss of the contractile power of the capillary, to defective blood-clotting, or to both. Contractile power is defective in thrombocytopenia, in which the capillary abnormality is associated with a shortage of platelets; in athrombocytopenic purpura, in which there is not a diminution in the number of platelets; and in haemorrhagic telangiectasia in which there is a sharply localized abnormality of the capillaries as regards failure to contract, the platelets and blood-coagulation being normal. In these conditions temporary pressure is an effective local measure, because a firm clot forms during its application. Defective blood-coagulation is responsible for

the haemorrhagic tendency in haemophilia, pseudo-haemophilia, fibrinopenia, some cases of haemorrhagic jaundice, and haemorrhagic disease of the new-born. In some conditions, notably jaundice and haemorrhagic disease of the new-born and also some rare haemorrhagic states, there may be a combined capillary and coagulation defect.

Haemorrhage

Transfusions of isinglass.—N. B. Taylor and E. T. Waters experimented with a 7 per cent solution of fish gelatin, or isinglass, in 0.9 per cent saline as a fluid for use in transfusion. Isinglass is soluble in water or saline, is non-toxic, and can be readily sterilized by boiling for 5 minutes. The authors found that, in animals in which the blood pressure had been lowered by bleeding, the transfusion of isinglass solution can restore the blood pressure and save the animals' lives.

Intravenous injections of sodium ascorbate.—C. P. Stewart, J. R. Learmonth, and G. A. Pollock found that in acute experimental haemorrhage in cats the benefit to be expected from the intravenous injection of cubic centimetres of a solution of sodium ascorbate is at least as great as that from a much larger volume of normal saline. In the authors' experiments, 8 out of 11 animals survived the strain of rapid bleeding to half the blood volume, and each of these 8 cats survived longer than 1 hour 40 minutes. The authors consider it possible that the action of the ascorbic acid is to secure a more adequate supply of oxygen to the tissues.

Crush Injuries

Clinical picture

Impairment of renal function.—The issue of the *British Medical Journal* for March 22, 1941, contains three papers and a leading article on this previously undescribed syndrome. E. G. L. Bywaters and D. Beall of the British Postgraduate Medical School describe 4 cases with necropsies. The patients had been buried for several hours with pressure on a limb. On admission they seemed in good condition except for swelling of a limb. But the haemoglobin was raised, the blood pressure fell and signs of renal damage followed, even though in 1 case the crushed limb was amputated; the output of urine, originally low, perhaps due to shock, diminished further, and the urine contained albumin and many dark-brown or black granular casts. Drowsiness and anxiety alternated, slight generalized oedema followed with thirst and vomiting. The blood pressure often remained slightly raised. The blood urea and phosphates progressively rose, and death often occurred somewhat suddenly within a week from the injury. Necropsy showed necrosis of muscles, and in the kidneys severe degeneration in the proximal convoluted tubules and, in the more distal part of the nephron, brown pigmental casts. The renal changes resemble those following mismatched blood transfusion (transfusion kidney); but after considering this possibility the authors conclude against this explanation. In 1 case the damaged limb was amputated; but it remains to be proved whether as an alternative immediate amputation of the crushed limb is the proper treatment to prevent the renal lesions and uraemia. The other two articles, each of a single fatal case, are on the same lines, one from St. Thomas's Hospital, by the authors of the first paper in collaboration with R. H. R. Belsey and J. A. R. Miles, and the other by R. Mayon-White and O. M. Solandt.

Treatment

Prolonged compression of limbs.—D. H. Patey and J. D. Robertson describe symptoms resulting from prolonged limb compression in a patient who had been buried under air-raid debris. The general condition of the patient at first was good, but after a few hours, shock set in accompanied by oedema of the limb, sensory disturbances, rising blood nitrogen, lowered alkali reserve, and anuria. The patient died in spite of treatment with intravenous plasma and serum. The cause of renal failure was obscure; to test the possibility that it was caused by a loss of substances from the blood into the decompressed limb and not to toxic substances released by the damaged limb, 2 other patients with the same injury were treated by compression of the limb by a wide blood pressure cuff. Intermittent pressure was applied to the first patient 11 days after admission when the above symptoms began to appear. After 1 day the urinary output was doubled, the swelling softened, and there was no thirst. A good recovery was made after further applications. Intermittent pressure was applied to the second patient within an hour of admission and maintained during waking hours with the arm held vertically. The initial good condition was maintained, the swelling softened and subsided after 2 weeks. It may be argued that the recovery was coincidental in both cases, but patients with similar symptoms often die. A parallel is drawn to the condition of shock after prolonged application of the tourniquet, and similar treatment is suggested.

Bites

Treatment

Human bites.—F. K. Boland, reviewing 60 cases of human bites in negroes, notes that the remarkable feature of such bites is the virulent destructive trauma which so often results from an apparently trivial wound. The three chief factors are the virulence of the pathogenic organisms, the method whereby the infection is conveyed along tendons and tendon sheaths, and the complicated arrangement of joint capsules and fascial planes which are difficult to free from infective processes. Radical treatment should be begun as soon as possible. If the wound has been sutured, it should be opened, and swabbed with phenol or packed with sulphanilamide crystals. At the same time sulphanilamide should be given by mouth. Old wounds require débridement.

Blows*Clinical picture*

Traumatic cardiac lesions.—E. Warburg, who in his monograph on subacute and chronic *Pericardial and Myocardial Lesions due to Non-penetrating Traumatic Injuries* (1938) analysed 189 collected cases of traumatic heart disease, now reviews a total of 225 well-established cases, one-third of which have been published in the last five years. The traumatic cardiac lesions include pericarditis, heart-block, myocardial damage, auricular fibrillation, and angina pectoris. Blunt non-penetrating blows over the heart must often cause pericardial haemorrhage or fibrinous exudation. Of traumatic auricular fibrillation the author collected 45 in his monograph, and now adds 10 fresh cases. In his present paper he quotes 16 cases of traumatic angina and 7 examples of traumatic coronary thrombosis.

H. Barber states that a blow over the heart may give rise to various heart lesions, such as symptomless cases with complete recovery, delayed rupture of the heart, clinical features of a disordered heart, haemopericardium, persistent myocardial weakness, heart-block, coronary thrombosis, myocardial injury in association with angina pectoris, auricular fibrillation, or rupture of a valve. Any part of the heart may be bruised or any of its chambers ruptured. The site of the lesion is not necessarily in relation to the situation of the blow. The anterior aspect of the right ventricle is most often injured. In many cases fractures of the bones of the thorax occur, and distress from this cause may mask the symptoms of heart disability.

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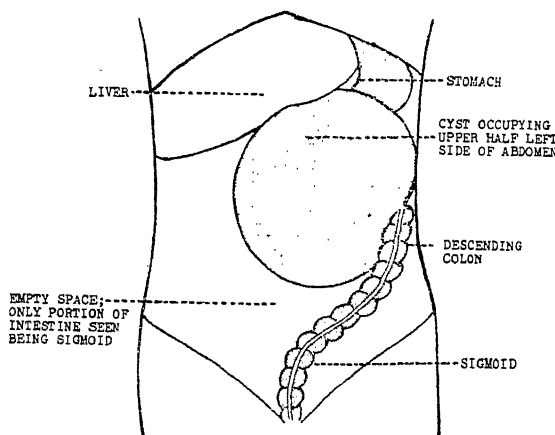
INTESTINAL OBSTRUCTION

See also B.E.M.P., Vol. VII, p. 221; Cumulative Supplement, Key Nos. 761-775; Surveys and Abstracts 1939, p. 387; 1940, pp. 12 and 353.

Acute Intestinal Obstruction

Clinical picture

Reversed rotation of the intestine accompanied by encapsulating peritonitis.—Under the above title J. W. G. Grant records a remarkable phenomenon, resembling an ovarian cyst, in a miner aged 62, whose abdomen was opened for acute intestinal obstruction. At first all that was seen was a large cyst with smooth shining white walls; it occupied most of the left hypochondrium, epigastrium, and left lumbar region. The only part of the intestine visible was the descending colon, which appeared to come from under the cyst in the left hypochondrium. This cyst, after it was cautiously opened, gave exit to foul-smelling blood-stained fluid and, after the opening was enlarged, was found to contain the whole of the intestine from the duodenum to the left colon, which was entirely free from adhesions to the inside of the cyst wall. The cyst wall was then removed from its attachment to the posterior abdominal wall. There was then found to be volvulus of the mid-gut loop, which had undergone rotation of about 270 degrees in a clockwise direction; this was undone. The distended caecum showed a gangrenous patch about the size of a shilling; a Paul's tube was fixed in this opening, the caecum was fixed in the abdominal wound, and this was closed. The incision healed after some suppuration, but a large opening, through which all the intestinal contents passed, persisted, and attempts to close it immediately caused intestinal obstruction; accordingly 13 weeks after the first operation, a further operation, hemicolectomy, union of the proximal end of the ileum, after division 5 or 6 inches from the ileo-caecal valve, with the sigmoid flexure, was successfully carried out, with a good recovery. Previous cases of this nature have been described as *péritonite chronique encapsulante* (P. Wilmoth and J. Patel) and *intestin sucre glacé* (Zuckergussdarm).



Diagnosis

Radiological examination.—P. B. Ascroft and E. Samuel report the results of the radiological examination of 57 patients with apparent acute intestinal obstruction, the diagnosis of which was verified by operation or necropsy, or both. When the intestine is obstructed the contents stagnate, absorption of water and gas diminishes, and an excessive amount of dilute secretion is poured out. Fluid and gas then separate readily, and fluid levels appear when the patient is in the erect position. These fluid levels are above the site of the obstruction, and are proportional in number to the duration of the obstruction and to its proximity in the small intestine to the ileo-caecal valve, and are divided into 4 grades. One to 3 fluid levels = grade 1; 4-8 = grade 2; 8-12 = grade 3; and more than 12 = grade 4. In 10 cases of obstruction of the ileum 6 were in grade 2, 2 in grade 3, and 1 in grade 4; the only case of obstruction in the jejunum was in grade 1. False fluid levels may be seen in the colon and perhaps in the terminal ileum when a watery enema is forced high up and not completely evacuated; it is therefore important to make the X-ray examination before an enema is given. The bearings of gas shadows and distension of intestinal coils are explained. The authors arrive at the following conclusions. (1) The combination of distinct fluid levels with a corresponding degree of distension of the small intestine with or without a similar condition in the colon is proof of obstruction, provided the clinical picture is compatible and is not seen in any other condition. (2) Serious obstruction is readily diagnosed radiologically, and is certainly excluded if absent. Plain films established the diagnosis of serious obstruction in every one of 30 cases subsequently confirmed. In 27 miscellaneous obstruction cases, clinically suspected of obstruction, a confident correct negative diagnosis was made in 22, and urgent obstruction excluded in the others. (3) Plain films consistently allow localization of the obstruction to the jejunum, ileum, or colon respectively. (4) Obstruction of the colon was localized correctly within a few inches of its actual position in 16 out of 19 cases. (5) Volvulus of the colon presents a characteristic picture in the plain films. (6) Contrary to some reports, considerable distension

of the small intestine (grade 2 or more) is frequent in obstruction of the colon. (7) There is a tendency to diagnose obstruction radiologically when it is absent. When X-ray signs are equivocal there is not any urgent obstruction.

General treatment

Intraperitoneal sulphanilamide.—R. V. Hudson, R. Smith, and F. R. Selbie, from analysis of 670 consecutive cases of acute intestinal obstruction, found that the fatality rate in cases in which simple release could be carried out was 6.7 per cent, whereas when resection was necessary the rate was 77.4 per cent. This high rate was mainly due to post-operative plastic peritonitis leading to mechanical obstruction; the causal micro-organism was *B. coli*. Experiments on rabbits showed that sulphanilamide introduced into the peritoneal cavity generally reduced, and in some cases even eliminated, the inflammatory process after resection of the intestine. Two cases of intestinal resection in man were treated with intraperitoneal sulphanilamide, and in neither was there any post-operative obstruction or peritonitis, local or general.

Miller-Abbott tube.—According to P. M. Glenn, the mortality from intestinal obstruction has been appreciably decreased by the use of the Miller-Abbott tube. Most gratifying results are obtained in post-operative cases complicated by peritonitis and obstruction. In pure paralytic ileus, decompression by means of the intestinal tube is the only uniformly reliable therapeutic measure. Good results are also obtained in all other types of intestinal obstruction, particularly in subacute or chronic obstruction. In cases of obstruction caused by a self-limiting disease, such as inflammation, intestinal intubation can sometimes obviate a surgical procedure. Contra-indications to the use of intubation are interference with the blood supply of the intestine, and external hernias.

Obstruction of the Small Intestine

Clinical picture

Primary carcinoma of the jejunum.—W. J. Craig reports a case of primary carcinoma of the jejunum in a woman, aged 48 years, with vomiting, pain below the right costal margin, tenderness in the epigastrium, but no palpable tumour. Radiological examination showed a narrowing of the jejunum 3 or 4 inches distal to the duodeno-jejunal junction; and a diagnosis of mechanical obstruction was made. The stomach and duodenal cap were normal. Nine inches of the jejunum were excised with an annular growth of the jejunum $3\frac{1}{2}$ inches from the duodeno-jejunal junction. No evidence of local metastasis was found. The tumour was a papillary, alveolar and tubular columnar-celled carcinoma involving all the coats of the intestine and ulcerated on the surface. Review of the recorded cases of primary carcinoma of the jejunum shows that the prognosis is poor, the average post-operative survival being one year.

Sarcoma.—The clinical picture may be much the same in primary sarcoma of the jejunum, of which L. K. Chont collected 31 cases and described cases of leiomyo-sarcoma; 10 of these cases occurred in the decade 51–60. Two groups of the tumours are described, (1) extrinsic, in which the area of attachment of the polypoid tumour to the outer wall of the intestine is small, does not encircle the intestine, and seldom causes obstruction, and (2) intrinsic, in which the polypoid tumour hangs in the lumen of the jejunum and is prone to induce intestinal obstruction.

Gas cysts.—J. A. Jackson reports a case of pneumatosis, or gas cysts, of the intestine, a rare condition of unknown origin. The patient presented the signs and symptoms of intestinal obstruction. At laparotomy a volvulus involving the ileum was found, and covering the greater portion of the intestine were innumerable cysts, varying in size from that of a millet seed to a size almost as large as that of the last phalanx of the thumb. The volvulus was reduced and a simple enterostomy performed. The author considers that gas gains entrance to the lymphatics at the site of an ulcer or a break in the gastro-intestinal mucosa, and is then distributed along the lymphatics to points between the layers of the intestinal walls in the form of cystic dilatations. The condition is self-limited and eventually undergoes a fibrous-tissue healing. It therefore does not require treatment *per se* when found together with a gastric or intestinal lesion at operation.

Obstruction by congenital bands.—R. Elman reports 3 cases of congenital intestinal obstruction caused by congenital bands with a twisting of the entire small intestine just distal to Treitz's ligament. These cases represented incomplete rotation and volvulus of the intestine. Ladd, who first described this condition, treated it by delivering the whole of the small intestine, untwisting it and cutting the bands, and obtained cure by this method. The most important symptom produced by the condition is persistent bile-stained vomiting, beginning shortly after birth, but in some cases interrupted by periods during which all food is normally retained. During periods of obstruction visible gastric peristalsis may be seen passing from left to right, as in pyloric stenosis. X-rays show no dilated loops of intestine, but a dilated stomach and duodenum can often be seen. There is no general abdominal distension, and the fullness in the upper abdomen can be made to disappear on aspiration by lavage of the gastric and duodenum contents.

Diagnosis

Congenital duodenal atresia.—S. Feggetter reports a case of congenital duodenal atresia in a female infant. The diagnosis of this rare condition rests on persistent vomiting, projectile or not, of bile-stained food soon after birth; relative constipation; fullness of the epigastrium;

and a typical radiogram, after a barium meal, which shows complete obstruction of the second part of the duodenum. In this case the abdomen was opened by a median supra-umbilical incision, and a posterior gastro-enterostomy was performed. The child made a satisfactory recovery.

- Ascroft, P. B., and Samuel, E. (1941) *Brit. J. Radiol.*, **14**, 11.
 Chont, L. K. (1941) *Radiology*, **36**, 86.
 Craig, W. J. (1941) *Brit. J. Radiol.*, **14**, 210.
 Elman, R. (1940) *Ann. Surg.*, **112**, 234.
 Feggetter, S. (1940) *Lancet*, **2**, 188.
 Glenn, P. M. (1941) *Amer. J. digest. Dis.*, **8**, 35.
 Grant, J. W. G. (1940) *Brit. med. J.*, **2**, 783.
 Hudson, R. V., Smith, R., and Selbie, F. R. (1941) *Lancet*, **1**, 438.
 Jackson, J. A. (1940) *Surg. Gynec. Obstet.*, **71**, 675.
 Wilmoth, P., and Patel, J. (1931) *J. Chir., Brux.*, **37**, 341.

INTESTINES, TUBERCULOSIS

See also B.E.M.P., Vol. VII, p. 253; and Surveys and Abstracts 1939, p. 389; 1940, p. 355.

Ulcerative Enterocolitis

Diagnosis

Phenolphthalein test.—L. E. Siltzbach and H. R. Nayer carried out 271 phenolphthalein (Woldman) tests on 206 patients to determine the value of the test in the detection of ulceration of the gastro-intestinal tract. Of these patients, 173 had active pulmonary tuberculosis and 33 were non-tuberculous. Necropsies on 33 of the cases showed that the test had a 'positive' error of 42 per cent and a 'negative' error of 19 per cent. The authors conclude that the test is not of any value in determining the presence or absence of tuberculous ulcers in the gastro-intestinal tract.

Siltzbach, L. E., and Nayer, H. R. (1940) *Amer. J. digest. Dis.*, **7**, 519.

JAUNDICE

See also B.E.M.P., Vol. VII, p. 261; Cumulative Supplement, Key Nos. 779–788; and Surveys and Abstracts 1939, p. 389; 1940, pp. 28 and 356.

Obstructive Hepatic Jaundice

Hypovitaminosis A and D

Prolonged dark-adaptation.—M. F. A. Woodruff and R. D. Wright describe a new photometer for measuring dark-adaptation. By means of this they demonstrated a prolonged adaptation time in cases of obstructive jaundice, and showed that this finding indicates deficient absorption of vitamin A. In cases of biliary obstruction the serum phosphatase is raised and the authors regard this as an indication of deficient absorption of vitamin D.

Prothrombin deficiency

Post-operative vitamin K deficiency.—S. C. Cullen, S. E. Ziffren, R. B. Gibson, and H. P. Smith state that the marked fall in the plasma prothrombin level which occurs post-operatively in patients with obstructive jaundice and biliary fistulae cannot be ascribed solely to the anaesthetic agent employed. The authors believe that, even when the patient suffers from vitamin K deficiency, the anaesthetic alone has little or no effect on the prothrombin level. Chloroform anaesthesia produces a fall in the prothrombin level in man, but neither ether nor cyclopropane anaesthesia produced any such effect in the uncomplicated cases investigated by the authors. The fall which occurs after operation in patients with obstructive jaundice or biliary fistulae is apparently due essentially to factors other than the anaesthetic agent itself.

Pre-operative administration of vitamin K.—J. Reid finds support for the opinion that defective absorption of vitamin K due to absence of bile salts in the intestine is chiefly responsible for prothrombin deficiency in obstructive jaundice, and biliary fistula before operation. It is suggested that prothrombin deficiency after operation in these conditions may be due to a deficient intake of vitamin K in the restricted post-operative diet. The routine pre-operative administration of vitamin K is recommended. The prothrombin deficiency in cirrhosis of the liver is considered to result from imperfect utilization of vitamin K by the liver. Prothrombin deficiency, even when severe, is not always associated with haemorrhage. It is considered to be responsible for the prolongation of haemorrhage after it has been caused by other factors, especially injury. The author found that a new water-soluble preparation, 2-methyl-1:4-naphthohydroquinone disuccinate, when injected intravenously, was as efficient as 2-methyl-1:4-naphthoquinone in increasing the amount of prothrombin in the blood. Its action appeared to be more rapid, though less sustained, than the latter, but a minor disadvantage was that it was not stable for long in aqueous solution, and so had to be dissolved in water immediately before use. The failure of patients with cirrhosis of the liver to respond to naphthoquinone compounds suggests that prothrombin estimations might be the basis of an additional test of hepatic insufficiency.

Cullen, S. C., Ziffren, S. E., Gibson, R. B., and Smith, H. P. (1940) *J. Amer. med. Ass.*, **115**, 991.

Reid, J. (1941) *Brit. med. J.*, **1**, 579.

Woodruff, M. F. A., and Wright, R. D. (1940) *Aust. N.Z. J. Surg.*, **10**, 135.

JOINTS, DISEASES AND DISORDERS

See also B.E.M.P., Vol. VII, p. 278; Surveys and Abstracts 1939, p. 390; 1940, p. 360; and p. 14 of this volume.

Pulmonary Osteo-Arthropathy*Clinical picture*

E. H. Rynearson and C. F. Sacasa record with a commentary an anomalous case of hypertrophic pulmonary osteo-arthropathy (acropachy) in a man, aged 43, who in 1937 showed signs of toxic goitre, and in the next year underwent subtotal thyroidectomy. Six weeks after this, progressive exophthalmos and post-operative myxoedema appeared, and later clubbing of the fingers and toes became noticeable. A diffuse, red, papular, confluent eruption appeared on the legs, arms, and scapular regions with secondary pustular infection in places. A blood bromide reading of 146 milligrams per cent was found on admission and after a week's treatment became normal; the rash was regarded as bromoderma with secondary pyogenic infection. The leucocyte count was 23,000 and the sedimentation rate was 115 millimetres at the end of an hour. Radiologically there was subperiosteal proliferation of the bones, of the hands, but not of the feet. Although this change is usually secondary to chronic intrathoracic suppuration, this is not essential; it may be associated with intrathoracic tumour, congenital and valvular morbus cordis, hepatic cirrhosis, and even without any primary disease, and this so-called idiopathic familial generalized osteophytosis has been described as having a tendency to a familial incidence. In about a third of the cases of hypertrophic pulmonary osteoarthropathy there are articular lesions, namely synovitis which may progress to erosion of the articular surfaces, and ankylosis. The authors' case associated with thyroid disease is the third of this kind to be recorded. H. M. Thomas, Jun. suggests that the sudden change from hyperthyroidism to hypothyroidism with the resulting circulatory alteration was responsible in his case.

Tuberculosis*Tuberculous ankle and tarsus*

Treatments compared.—W. R. D. Mitchell, discussing the end-results and treatment of tuberculous disease of the ankle and tarsus, states that, of 23 patients treated conservatively by immobilization of the ankle in recumbency, 8 (about 35 per cent) died with tuberculous disease in other parts of the body. Of 14 patients treated by early amputation within 1 year of onset of the disease, 13 were living, all with a reasonable expectation of life. Early amputation shortens the period of disability, removes the primary lesion and prevents secondary infection, obviates the worry and mental changes produced by a long illness, and lowers expense of hospital treatment. The author recommends that, in patients over 45 years of age, amputation should be performed through the upper tibia without delay. In patients aged 17 to 35 there should be a 6-months' trial of conservative treatment by immobilization of the ankle in recumbency in an open-air hospital. If the lesion then shows definite signs of healing, a further period, under strict observation, may be prescribed. If, at any time, progress becomes arrested for more than 3 months, amputation should be performed immediately. In patients aged 35 to 45, amputation should be considered if there is any doubt as to the patient's general condition.

Tumours of the Synovial Membrane*Clinical picture*

Malignant synovioma.—C. W. Hutchison and D. H. Kling report a case of malignant synovioma arising from a bursa at the medial aspect of the knee-joint. Repeated excision and X-ray therapy failed to prevent local recurrences and pulmonary metastases. Death occurred 7 years after the onset of symptoms. The primary tumour as well as the metastases showed the complex structure typical of synovial tumours, consisting partly of cystic and cleft-like spaces lined by papillomatous growths of glandular structure, containing one or several rows of large polygonal cells. The lumen contained a viscid, mucous, synovial fluid.

Traumatic granuloma.—J. K. Stack states that tumours of the synovial membrane are rare, but, when they arise, they involve the knee more often than any other joint. The author reports a synovial granuloma which, despite its simple and benign nature, caused recurrent spontaneous bleeding into the joint cavity. It was apparently of traumatic origin, but its subsequent growth and clinical course took it out of the category of the ordinary synovial impingement, which may cause transient symptoms after trivial injuries.

Hutchison, C. W., and Kling, D. H. (1940) *Amer. J. Cancer*, **40**, 78.

Mitchell, W. R. D. (1940) *Brit. J. Surg.*, **28**, 71.

Rynearson, E. H., and Sacasa, C. F. (1941) *Proc. Mayo Clin.*, **16**, 353.

Stack, J. K. (1940) *J. Bone Jt Surg.*, **22**, 735.

Thomas, H. M., Jun. (1933) *Arch. intern. Med.*, **51**, 571.

KALA-AZAR

See also B.E.M.P., Vol. VII, p. 330; and Cumulative Supplement, Key No. 826; Surveys and Abstracts 1940, p. 362; and p. 100 of this volume.

Treatment*4:4'-diamidinostilbene*

R. Kirk and M. H. Sati employed 4:4'-diamidinostilbene in 8 cases of Sudan kala-azar.

Of these patients 2 died and the other 6 appeared to recover without any tendency to relapse during an observation period of 4 months. The patients who died were moribund when they came under treatment, and died after they had received only 3 and 5 doses of the drug respectively. The concentration of the drug employed was 100 milligrams in 10 cubic centimetres of distilled water. The dose, which was given intravenously daily or on alternate days, varied from 1 to 2.6 milligrams per kilogram of body weight. The total dosage required to effect an apparent cure varied considerably; one patient received a total of 975 milligrams in 24 injections given for 5 weeks; another patient received more than 70 injections during a period of 6 months. Toxic symptoms were negligible, and consisted of epigastric discomfort with breathlessness and dizziness. Three months later the authors report further investigations on the effect of 3 aromatic diamidines in 44 cases of Sudan kala-azar, and found that the results obtained compared favourably with those previously recorded with other methods of treatment. In 28 cases treated by 4 : 4'-diamidinostilbene the immediate recovery rate was 86 per cent. In 13 cases treated with 4 : 4'-diamidino-diphenoxypentane the immediate recovery rate was 75 per cent. Two cases were treated with 4 : 4'-diamidinodiphenoxypropane, with 1 death. A patient, apparently resistant to antimony, improved rapidly when the treatment was changed to 4 : 4'-diamidinostilbene. The dose given at each injection varied from 1 to 2.6 milligrams per kilogram of body weight, and was given intravenously. In therapeutic doses the toxicity was low.

Kirk, R., and Sati, M. H. (1940) *Ann. trop. Med. Parasit.*, **34**, 83 and 181.

KELOID

See also B.E.M.P., Vol. VII, p. 366.

Aetiology

According to H. P. Pickerill the formation of a keloid is due to the coincidence of several factors in a wound some of which can be prevented. The factors are: (1) the destruction of the subcutaneous tissue whereby the scar becomes attached to the adjacent muscle. This is bound up with the factor of tension and movement. (2) A scar or incision the long axis of which lies in the direction of the subjacent muscle fibres is more likely to become keloid than one which is transverse. (3) The inclusion of oil globules in the healing wound is a direct agent in the promotion of keloid formation, probably because of its chemotactic effect on certain of the cells of the reticulo-endothelial system.

Pickerill, H. P. (1940) *N.Z. med. J.*, **39**, 327.

KIDNEY, SURGICAL DISEASES

See also B.E.M.P., Vol. VII, p. 380; Cumulative Supplement, Key Nos. 829–840; and Surveys and Abstracts 1939, p. 393; 1940, pp. 118 and 363.

Congenital Abnormalities

Fusion of the kidneys

J. Swift Joly suggests a simple classification of fused kidneys. (1) Complete fusion; the united mass shows little or no evidence, except that the renal pelves are double, that it is due to the union of 2 distinct organs. It may form an irregular mass, or more often be roughly quadrilateral with rounded edges, like a ship's biscuit (*rein en galette*), or it may be a round or oval mass, or very irregular with a lobulated surface. Fused kidneys are always ectopic and never above the level of the 4th or 5th lumbar vertebra; they do not undergo the ascent or rotation of the normal kidneys and both renal pelves are on the anterior surface and at some distance from each other. The blood supply is always irregular. The congenital anomaly occurs at a very early stage of development, before the kidneys leave their primitive position in the pelvis. (2) Incomplete fusion: (a) fusion of similar poles—the horseshoe kidney, in the usual form, occurring once in every 143 operations on the kidney; the lower poles are united over the bifurcation of the aorta. Usually the lateral masses are ovoid and equal in size, but they may be unequal from congenital hypoplasia of one kidney and the renal tissue then resembles the shape of the letter L. The condition is now generally diagnosed by pyelography. In about 20 published cases the upper poles are united—the 'reversed horseshoe kidney', or 'the horseshoe kidney with the concavity looking downwards'. (b) Fusion of dissimilar poles: there may be fusion of the upper pole of one kidney with the lower pole of the other kidney. These end-to-end fusion kidneys have been split up into smaller groups, the 'sigmoid', in which the long axes of the combined mass is not vertical, but is inclined from above downwards and inwards so that a considerable part, if not the whole, of the lower kidney lies on its own side of the body; the ureter from the upper kidney runs a normal course, and that from the lower kidney lies entirely on its own side. The 'long' kidney is similar to the 'sigmoid', except that it lies entirely on its own side of the body; its appearance varies considerably. The term 'L-shaped' has also been applied to some end-to-end fusions. But Joly regards this further classification as unnecessary.

Polycystic Disease

Clinical picture

Fatal end by uraemia.—W. Doolin reports the death from acute uraemia, 3 days after an injury with much bruising and laceration of the deltoid muscle, of a man aged 54 years who previously had seldom been ill for a day. At the necropsy congenital polycystic disease of

the liver and to a high degree of the kidneys was found. The acute uraemia was ascribed to the absorption of the extravasated proteins from the blood in a haematoma and the torn muscle, their subsequent excretion by the kidneys being too great a physiological strain for these organs which had responded without protest to the stresses of an active outdoor life. The comparative rarity of this well-known condition of congenital polycystic disease of both kidneys is shown by Thomson-Walker's quotation that out of 389,773 admissions to the London Hospital in the years, 1900–1924 there were only 79 cases found clinically, or 1 in 4,933. It is said that in slightly more than half the cases death is due to terminal uraemia, the majority of the deaths occurring between the ages of 40 and 60, and that few of the patients live longer. Clinically the cases are divided into two groups, those proving fatal soon after birth and those in which patients survive; but pathologically they are the same.

Injuries

Post-operative damage

Accidental bilateral ligation of the ureters.—F. Pilcher, Jun. and A. E. Aikenhead record the case of a woman, aged 34, who underwent, for menorrhagia and metrorrhagia of 3 years' duration, removal of the uterus and uterine (Fallopian) tubes. Her immediate post-operative condition was good although in the night 3 oz. only of urine were passed, and then there was anuria with an empty bladder. Investigations pointed to operative damage and obstruction of both ureters. On the third day the non-protein nitrogen was 80 milligrams per 100 cubic centimetres of blood, and the patient was drowsy, listless, and complained of headache. The right kidney was then exposed and seen to be dusky and tensely swollen; the ureter which was dilated was drained by a catheter, 224 oz. of urine being thus passed in the next 24 hours. Seven days after the first operation similar drainage of the left kidney was carried out and eventually both ureters became patent, and 10 months after the hysterectomy the urinary tract was shown by a thorough urological examination to be quite normal. The authors are convinced that such accidents are much more frequent than their records; injury to the ureters is said to occur in 15 per cent of operations on the female genital tract, most commonly during total abdominal hysterectomy, especially when done for cancer, or large cervical and intra-ligamentous fibroids; next comes vaginal hysterectomy. When the damage is unilateral, the silent formation of a hydronephrosis may be overlooked. There are two possible forms of treatment for bilateral ureteral obstruction: nephrostomy, which the authors performed and prefer, or deligation. If the catgut sutures have completely obstructed the ureters the patient will die of uraemia before the catgut is absorbed and the lumen of the ureters restored.

Calculi

Aetiology

Factors in calculus formation.—M. L. Boyd reports 4 cases with multiple small phosphatic stones and sand in the kidneys; of these 3 had had poliomyelitis with rather extensive paralyses, and the fourth had a fractured femur which would not unite satisfactorily. A stereoscopic urogram of the latter showed that the minor calyces of the left kidney pointed dorsally from the major calyces, which in turn pointed back from the renal pelvis; a somewhat similar condition existed in the right kidney. The stones had obviously accumulated in the kidneys because of this condition, and because the patient had not lain on the abdomen, which may have been an important factor in the occurrence of calculi in bedridden patients.

Clinical picture

Containing lead.—M. Trumper and S. T. Gordy report the case of a negro, aged 46, from whom at operation a renal calculus was removed which on examination was found to contain 3 per cent of lead. Analysis of the urine showed it to contain 0.054 milligram of lead per litre. The patient had been exposed to lead dust in his occupation for 5½ years, and had some shot-gun lead pellets embedded in his arm, leg, and thigh; these pellets had been present for 23 years. This appears to be the first report of a urinary calculus containing lead.

Ureteral calculi

Surgical removal.—R. T. Bergman contributes an article on the surgical removal of low-lying ureteral stones by the vaginal route and recommends the following technique: The patient is placed in the extreme lithotomy position, and while under anaesthesia an attempt is made to palpate the stone vaginally. If orientation is difficult, a catheter inserted in the ureter may serve as a guide. Flexible retractors are then placed in the vagina. The cervix is grasped with a tenaculum forceps, and traction made to gain better access to the stone by bringing the base of the bladder and ureter into the field. The incision is transverse, generally 3 to 4 cubic centimetres long, and anterior and lateral to the cervix through the vaginal mucosa, and thus is made directly over the stone, if it is palpable. The incision is further deepened with blunt dissection carried out by forceps, and the finger then introduced should palpate the stone. The ureter is grasped by an 8-inch Babcock forceps placed above the calculus, if possible, to prevent its slipping up the ureter. With the ureter thus exposed, a longitudinal incision is made through the ureteral wall, and the calculus removed. Fine chromic catgut is used to suture the ureteral incision, and the vaginal incision is left open for drainage.

Treatment with avertin.—M. E. Greenberger and J. Birnbaum employed avertin in 31 cases of ureteral calculi, with delivery of the calculus within a few days. One or two catheters are, if possible, passed beyond the stone, and allowed to remain *in situ* for 48 hours. After this

period 5 to 20 cubic centimetres of a freshly made 2 per cent solution of avertin are introduced through the catheters, the catheters are plugged, and the solution is allowed to remain for 15 minutes. During this time the patient remains in the sitting position. The catheters are then slowly withdrawn, and at the same time an additional 3 to 5 cubic centimetres of avertin solution are injected. The solution consists of 1 gramme of avertin crystals dissolved in 50 cubic centimetres of warm distilled water.

Tumours

Primary carcinoma of the ureter

Clinical picture.—E. N. Cook and V. S. Counseller state that though primary carcinoma of the ureter is comparatively rare, it occurs sufficiently often to raise the possibility that it is responsible for hydronephrosis, especially if associated with haematuria. The outstanding symptom is haematuria, and the blood in the urine is often bright red. Excretory urograms show the extent of the pyelectasis, calyctasis, and ureterectasis present. Retrograde pyelograms are essential to demonstrate the lesion in most cases, and should be made whenever patients with hydronephrosis are of 'cancer age', if the cause is not definitely known.

F. Pilcher and D. S. Macnab record a case of primary carcinoma of the lower end of the right ureter in a man, aged 56 years, and review the recorded cases. This is described as one of the rarest sites for primary carcinoma. A. G. Foord and P. A. Ferrier (1939) collected 139 cases, and Pilcher and Macnab have now brought the total up to 155. The average age is 55 years, the sex incidence about equal, and in two-thirds of the cases the growth is in the lower third of the ureter. The tumour felt is generally the hydronephrotic kidney, the ureteral carcinoma being seldom palpable. The outstanding symptoms are haematuria, pain, and a tumour; but the only pathognomonic sign is a filling defect in the ureterogram. Clinically and histologically the ureteral growth resembles the primary forms occurring in the urinary bladder. The treatment is complete nephro-ureterectomy, preferably in two stages: removal of the lower tumour-containing segment, followed later by nephrectomy.

Nephro-ureterectomy.—H. M. Stang and A. J. Hertzog report 4 cases of primary carcinoma of the ureter. The chief manifestations were haematuria and lower abdominal pain; in 3 of the cases cystoscopy showed a growth protruding from the ureteral orifice, and ureterograms showed dilated ureters at the site of the growth. The average age of the patients was 58.2 years. The treatment is complete nephro-ureterectomy, including a portion of the bladder wall surrounding the meatus, either in a one or two-stage procedure. Post-operative irradiation should be given.

Renal tumour

Fever as initial symptom.—E. J. McCague reports a case of renal tumour in a woman, aged 47, in whom the well-known triad of haematuria, pain, and a palpable abdominal mass was absent. The only clinical manifestation was an obscure fever of 1 year's duration, accompanied by nausea, vomiting, and irregular uterine bleeding from multiple fibroids. A review of the reported cases showed that fever as the initial and only symptom of renal tumour has seldom been recorded.

Hypernephroma.—H. E. Carlson and N. F. Ockerblad report a case of hypernephroma with a history of haematuria of 10 years' duration. A comparison of pyelograms taken at an interval of 9 years showed in both the characteristic picture of a renal tumour, with definite evidence of considerable growth in the intervening years.

Diagnosis

General survey.—E. Smith and A. Young analyse 118 primary tumours of the kidney seen at Montreal during 20 years; 21 were benign; all but one of these were from patients who had been operated upon, and of these 20 there were 8 solitary cysts. These innocent tumours, not including the solitary cysts, have not any characteristic symptoms to distinguish them from malignant growths of the kidney, and were diagnosed as benign before operation. The malignant tumours numbered 97, the largest number (39) occurred in the decade 50 to 60; 19 patients showed metastases and therefore were not operated upon; 9 were not operated upon because of their poor physical state, and 7 refused operation. The right kidney was involved in 47 and the left in 50 cases. The approximate percentages of the site of the growth were: the whole kidney 25, the upper pole 25, the lower pole 18, the middle area 16, and the renal pelvis 16. The pathological reports on the 62 patients operated upon were adenocarcinoma in 40, carcinoma in 15, sarcoma in 3, embryoma (Wilms) in 2, and papillary carcinoma of the renal pelvis in 2. In a few, only 3, the growth was entirely confined to the kidney; unfortunately extension occurred into the surrounding tissues and involved the peri-aortic lymphatic glands. The symptom-triad of haematuria, pain, and tumour was present in 19 patients, most of whom had metastases and were considered to be unsuitable for operation. Haematuria was the most prominent initial sign in half the cases; pain was the initial symptom in 34 cases, and tumour an initial sign in 9 cases. In 4 cases haematuria was the only sign, and in 25 cases it did not occur. With the help of the pyelogram and the cystoscope the diagnosis was generally not difficult. Intravenous urography, which at first was thought would be useful in securing an earlier diagnosis, proved disappointing. The prognosis was bad; the great majority of the patients died from metastases or recurrences within 5 years.

Renal metastases

Incidence.—B. S. Abeshouse and A. E. Goldstein, stimulated by observations of a primary

growth in one kidney with metastases in the other kidney, review 1,458 collected cases of metastatic malignant disease of the kidney, and record 23 personal cases. They conclude that the kidneys are a relatively uncommon site of malignant metastases. The actual number of cases of renal metastases associated with carcinoma (947) is more than 5 times that associated with sarcoma (176). But from a comparative point of view it appears that the relative incidence of renal metastases in sarcoma is about twice that in carcinoma. Although there is not any primary growth from which metastases occur solely in the kidney, sarcomas, especially the lymphoblastomas, are more often found in the other kidney. A detailed analysis of a large number of renal metastases as regards the character and site of the primary growth showed that metastatic renal tumours are most often associated with primary neoplasms of the kidneys (26.5 per cent), and less frequently with primary growths of the lung (15.6 per cent), skin (6.3 per cent), and oesophagus (6 per cent).

Metastatic ureteral carcinoma.—J. A. Lazarus reports a case of metastatic ureteral obstruction as a result of carcinoma of the ovary. Including the author's case, only 18 cases of metastatic tumours of the ureter have been recorded. In this case malignant changes were found in a dermoid cyst of the ovary. The differentiation of metastatic from primary tumours of the ureter can only be made histologically by finding tumour cells in the perivascular lymph spaces, or within the vessels of the ureter.

Abeshouse, B. S., and Goldstein, A. E. (1941) *Urol. cutan. Rev.*, **45**, 163.

Bergman, R. T. (1941) *J. Urol.*, **45**, 176.

Boyd, M. L. (1941) *J. Amer. med. Ass.*, **116**, 2245.

Carlson, H. E., and Ockerblad, N. F. (1941) *Amer. J. Roentgenol.*, **45**, 221.

Cook, E. N., and Counsellor, V. S. (1941) *J. Amer. med. Ass.*, **116**, 122.

Doolin, W. (1941) *Brit. J. Surg.*, **28**, 500.

Foord, A. G., and Ferrier, P. A. (1939) *J. Amer. med. Ass.*, **112**, 596.

Greenberger, M. E., and Birnbaum, J. (1941) *Urol. cutan. Rev.*, **45**, 301.

Joly, J. Swift (1940) *Proc. R. Soc. Med.*, **33**, 697.

Lazarus, J. A. (1941) *J. Urol.*, **45**, 527.

McCague, E. J. (1940) *Arch. Surg., Chicago*, **41**, 385.

Pilcher, F., Jun., and Aikenhead, A. E. (1940) *Canad. med. Ass. J.*, **43**, 436.

— and Macnab, D. S. (1941) *Canad. med. Ass. J.*, **44**, 361.

Smith, E., and Young, A. (1941) *Canad. med. Ass. J.*, **44**, 149.

Stang, H. M., and Hertzog, A. J. (1941) *J. Urol.*, **45**, 519.

Trumper, M., and Gordy, S. T. (1941) *J. Amer. med. Ass.*, **116**, 1389.

LABOUR: NORMAL LABOUR

See also B.E.M.P., Vol. VII, p. 417; Cumulative Supplement, Key Nos. 841–844; Surveys and Abstracts 1940, p. 371; and p. 16 of this volume.

Factors in Labour

Onset of labour

Oxytocic substance and pituitrin.—The presence in the blood of pregnant women of pituitrin and an oxytocic substance has been claimed by some authors to be the cause of pregnancy toxæmias and the cause of the onset of labour. J. E. Lackner and A. S. Tulskey have failed to demonstrate the presence of such substances. They collected approximately 250 cubic centimetres of blood from each of 13 women in labour, 5 of whom had had moderate or severe toxæmia. The serum collected from these blood samples was tested by injection into normal women in whom uterine contractions were recorded by means of the intra-uterine bag. In no instance was a distinct response obtained to the serum, and the authors therefore conclude that the blood serum of women in labour either contains no oxytocic substance or an amount too small to be detected by this method.

Lackner, J. E., and Tulskey, A. S. (1940) *Endocrinology*, **27**, 41.

LABOUR: CONTRACTION AND DEFORMITY OF THE BONY PELVIS

See also B.E.M.P., Vol. VII, p. 490.

Course of Labour

Prolapse of cord

W. F. Mengert and F. H. Longwell, in a series of 9,546 deliveries, found that prolapse of the umbilical cord occurred in 0.61 per cent of babies weighing 1,500 or more grammes at birth. The percentage incidence among the various presentations was: cephalic 0.37, breech 4.54, and transverse 14.27. The foetal mortality rate was 46.6 per cent, but no mothers died. The death-rate of babies of primigravidae was almost twice that of babies of multigravidae. When the presenting part at the time of the prolapse was at the inlet, the mortality was 66.6 per cent, at mid-pelvis 43.4, and at outlet 37.5. When the cervix was less than 5 centimetres dilated the mortality was 63.8 per cent, between 5 and 10 centimetres 41.7 per cent, and completely dilated 36.7 per cent. The average length of the prolapsed cords was 73.0 centimetres. Among 545 patients with cords 75 or more centimetres long, prolapse occurred 6 times as often as among the entire obstetrical service.

Mengert, W. F., and Longwell, F. H. (1940) *Amer. J. Obstet. Gynec.*, **40**, 79.

LABOUR: OBSTRUCTIONS IN THE SOFT PASSAGES

See also B.E.M.P., Vol. VII, p. 511; and Surveys and Abstracts 1939, p. 394; 1940, p. 373.

Obstructions in the Cervix*Failure of dilatation of os*

P. J. Carter states that the so-called condition *conglutinatio orificii externi* is an unusual cause of delayed labour. The condition is not a true conglutination, but rather a failure of dilatation of the circular fibres around the external cervical os. The opening in the cervical os cannot always be identified, even by speculum examination. Artificial measures are generally necessary to relieve the condition which sometimes terminates in spontaneous delivery, but may result in prolonged dystocia, amputation of the cervix, or rupture of the uterus. As a rule all that is necessary is entrance into the cervical canal by continuous gentle digital pressure against the external os. In some cases Caesarean section is necessary.

Carter, P. J. (1941) *Amer. J. Obstet. Gynec.*, **41**, 606.

LABOUR: OPERATIVE AND MANIPULATIVE PROCEDURES

See also B.E.M.P., Vol. VII, p. 533; Surveys and Abstracts 1939, p. 395; 1940, p. 374; and p. 16 of this volume.

Induction of Labour*Alkalinization and pituitary extract*

According to R. V. Boedeker the gravid human uterus responds more favourably to posterior pituitary extract after alkalinization. In a series of 94 cases he gave 40 grammes of sodium bicarbonate by the mouth in doses divided over the 24 hours, beginning the day before the attempted induction of labour. After this alkalinization treatment, patients were given a hot soap solution enema, followed immediately by 2 minim doses of posterior pituitary extract at 20-minute intervals for a maximum of 8 doses, or until labour was established. Of the 94 inductions attempted, 65, or 70 per cent, succeeded. In a control group of 113 women, 46, or 44.6 per cent, passed into labour. It seemed that a necessary corollary would be that the gravid human uterus after acidification is relatively less responsive to posterior pituitary extract; this observation was carried out in 20 cases but the induction was successful in 3, or 15 per cent, only. Toxic effects were not noted in any of these trials.

Posterior pituitary extract

R. S. Siddall and D. G. Harrel, discussing the use of posterior pituitary extract during the first stage of labour, maintain that, although large doses are admittedly dangerous, small doses may be given with reasonable safety in a prolonged first stage due to poor pains. Of 62 such cases, posterior pituitary extract produced efficient and lasting pains in 42. Some of the patients were given two or more courses of repeated doses. The initial dose of posterior pituitary extract should not be larger than 1 minim, or 0.059 millilitre.

D. P. Murphy gave 375 hypodermic injections of posterior pituitary extract, not exceeding 3 minims (0.1776 millilitre) per dose, to 96 women at various stages of pregnancy. During treatment a continuous record was made of their uterine contractions with a Lóránd tocograph. Forty-seven per cent of the patients did not respond. An increased response was more frequent (1) in multigravidas than in primigravidas, (2) during than before labour, (3) later in pregnancy than earlier, (4) after the larger than the smaller doses of pituitary extract, and (5) when the uterine wall was tense than when it was relaxed. The author concludes that the amount of posterior pituitary extract employed, and the degree of tension of the uterine wall at the time of treatment are important factors to be considered. During pregnancy and labour the most efficient type of uterine contraction is produced by the administration of small doses.

High puncture of the membranes

Coralie R. Short reports 87 consecutive cases in which labour was induced by high puncture of the membranes. In most of the patients labour was induced at 39 weeks or later; in none before 36 weeks. An anaesthetic was not necessary. With the patient in the lithotomy position, the vulva and surrounding parts were carefully cleansed with dettol. A catheter was passed. Then a Sims's speculum was placed in the vagina, which was again washed out well with dettol. The cervix was gently dilated, and the membranes when possible were separated from it by running the finger round inside the internal os. A special catheter was then passed, and the membranes punctured above the head. About 15 to 20 ounces of liquor amnii were generally drawn off. In some cases labour started at once and in a large percentage of cases in less than 24 hours.

Evisceration and Embryotomy*Foetal ascites*

E. T. Ellison reports a case of obstructed labour due to foetal ascites. Prenatal physical examination suggested the presence of abnormal uterine contents. The head was delivered by low forceps after an episiotomy. The shoulders appeared to be caught by what was known to be an adequate pelvis. It was necessary to do a bilateral cleidotomy which quickly facilitated delivery of the shoulders. After the head and shoulders had been delivered and the amniotic fluid drained off examination showed that there was still a large abdominal tumour, which prevented extraction of the foetus. A large foetal abdomen was felt on manual examination.

This was punctured with Smellie's scissors and a large amount of clear yellow fluid containing some fibrin flakes drained out.

Boedeker, R. V. (1941) *Amer. J. Obstet. Gynec.*, **41**, 84.

Ellison, E. T. (1940) *Amer. J. Obstet. Gynec.*, **40**, 1057.

Murphy, D. P. (1941) *Amer. J. Obstet. Gynec.*, **41**, 274.

Short, Coralie R. (1940) *Bristol med.-chir. J.*, **57**, 121.

Siddall, R. S., and Harrel, D. G. (1941) *Amer. J. Obstet. Gynec.*, **41**, 589.

LABOUR: ANAESTHESIA AND ANALGESIA

See also B.E.M.P., Vol. VII, p. 573; Surveys and Abstracts 1939, p. 396; 1940, pp. 19 and 375; and p. 16 of this volume.

Anaesthesia and Analgesia

Methods of administration

Paraldehyde analgesia with perineal anaesthesia.—C. K. Fraser and J. W. Jones claim good results from the use of paraldehyde analgesia with perineal anaesthesia in terminating the second stage of labour. The perineal anaesthesia is effected as follows. A point on the skin midway between the rectum and ischial tuberosity is selected for the entrance of the needle. A 22-gauge needle, 10 centimetres long, is inserted at the selected area and directed just medial to the ischial tuberosity. With one finger in the vagina, the point of the needle is guided posteriorly to the ischial spine, care being taken not to pierce the vaginal wall. The needle is brought to rest proximally and posterior to the ischial spine. Traction is made on the plunger and if blood is not aspirated 10 cubic centimetres of a 1 per cent solution of procaine hydrochloride is injected. By withdrawal of the needle for 2 or 3 centimetres, some of the solution is deposited beneath Colles's fascia where the arrangement of fascia only allows the solution to escape anteriorly where it bathes the terminal branches of the pudendal nerve anterior to the triangular ligament. The needle is then withdrawn until the point is just under the skin; it is then inserted in order to infiltrate the cutaneous and mucosal surfaces at the site of the perineotomy, and 10 cubic centimetres of the solution are injected. The procedure is then repeated on the opposite side, omitting the local infiltration for incision. By this method 50 to 60 cubic centimetres of the solution are adequate.

Use of Sedatives

Evipan soluble

H. E. Anderson and G. P. Bohlender report on the use of evipan soluble (hexobarbitone soluble) during labour, and find that it is a safe and effective analgesic. The hypodermic injection of $\frac{1}{100}$ grain (0.0004 gramme) of scopolamine hydrobromide greatly enhanced the analgesic effect of evipan. The initial dose of evipan was 1 gramme, given per rectum, and obtained by using 30 cubic centimetres of a solution of 3 grammes (46.2 grains) of evipan in 90 cubic centimetres of tap water. If, after one or two hours, it was thought necessary, 0.5 gramme (7.7 grains) or 1 gramme (15.4 grains) was given. This treatment was given when the woman was unquestionably in labour, when she began to complain of pain, and when the os was 3 centimetres, or more, dilated. The drug did not generally delay labour, and gave excellent analgesia. There were no gross ill effects on the baby.

Anderson, H. E., and Bohlender, G. P. (1941) *Amer. J. Obstet. Gynec.*, **41**, 305.

Fraser, C. K., and Jones, J. W. (1940) *Amer. J. Obstet. Gynec.*, **40**, 506.

LABOUR: RADIOLOGY

See also B.E.M.P., Vol. VII, p. 584; and Cumulative Supplement, Key Nos. 897-908.

Technique of Routine Examination

Soft tissue radiography

Placental implantations.—A. L. Dippel and W. H. Brown, employing soft tissue radiography in 259 patients in 261 pregnancies, obtained clear visualization in 236 cases, or 90 per cent. The chief factor interfering with visualization was hydramnios, and accounted for non-visualization in 5.73 per cent of the X-rays. Unsatisfactory films were obtained in 3.05 per cent of the cases, and it was impossible to visualize the placenta in 2 of 8 cases of twin pregnancy. Immaturity, provided the pregnancy has advanced beyond midpoint, and abnormal presentations and positions are not inhibiting factors in visualization. Calcification of the placenta was rarely so extensive as to be useful in localization of the placental site. The placental implantations were almost equally divided between the anterior and posterior walls of the fundus. With low implantations, however, about 8 times as many placentas were found implanted on the anterior as on the posterior wall of the lower uterine segment. Only 11, or 12 per cent, of 92 cases of vaginal bleeding, examined radiographically and clinically, showed true placenta praevia; in 15 other cases there was merely X-ray evidence of low implantation of the placenta, without the usual clinical signs.

Visualization of placenta.—According to A. L. Dippel and W. H. Brown, the placenta can be visualized by soft-tissue radiography in a high percentage of cases. This is a valuable aid in cases of suspected placenta praevia, and generally obviates the necessity of vaginal examination. The technique employed is one of high voltage and low exposure time. The milliamperesecond ratio used is 50 to 4. The voltage (peak) is varied between 65 and 85 kilovolts, according to the obesity of the patient.

Dippel, A. L., and Brown, W. H. (1940) *New Engl. J. Med.*, **223**, 316.

— (1940) *Amer. J. Obstet. Gynec.*, **40**, 986.

LACRIMAL APPARATUS DISEASES

See also B.E.M.P., Vol. VII, p. 592; Cumulative Supplement, Key No. 913; and Surveys and Abstracts 1939, p. 397.

Diseases of the Lacrimal Gland

Tumours

Boeck's sarcoid.—J. Rosenbaum reports a case of Boeck's sarcoid of both lacrimal glands, the right being the larger, in a woman aged 26. The condition was diagnosed as enlargement of the accessory lacrimal glands. The Wassermann, Kahn, and Mantoux tests were negative. When first seen the lymphatic glands in the neck and around the angle of the jaw were enlarged. After excision of the right accessory lacrimal gland which showed granulomatous inflammation with some giant cells, there was a distinct diminution in size of the corresponding gland on the left side. The patient underwent tonsillectomy. Four months later she complained of enlarged lymphatic glands in both inguinal regions and the posterior triangle in the neck on the right side. A small lymphatic gland was removed from the posterior triangle in the neck for biopsy; histologically the gland showed multiple small tubercle-like areas of epithelioid cells surrounded by collagenous fibrous tissue. There were occasional giant cells, but little coagulation necrosis. It does not appear that the presence of tubercle bacilli was excluded, but the report continued, 'the picture conformed to that of the so-called fibroid type of tuberculosis which is now recognized as one of the tissue-reactions found in sarcoidosis'.

H. B. Stallard reports a case of Boeck's sarcoidosis of the lacrimal gland in a woman of 45. A lump, 2.75 by 1.75 centimetres, removed from the right lacrimal gland, was composed of masses of endothelioid cells arranged irregularly, with collagen material and red blood cells between some of the cells. Around these cellular masses were considerable aggregations of lymphocytes.

Treatment

Dacryocystitis of the new-born.—A. Busacca recommends irrigation of the lacrimal sac with about 2 cubic centimetres of bouillon containing Besredka filtrates, in dacryocystitis of the new-born. After anaesthetization with cocaine, a fine blunt cannula is introduced into the lower lacrimal punctum, and the liquid injected with as much pressure as possible. Irrigations are repeated every second day. They do not cause any reaction, and only rarely produce any oedema, in which event a longer interval is allowed between treatments. In many cases restoration of the lumen of the naso-lacrimal canal is obtained by this method.

Busacca, A. (1940) *Arch. Ophthalm., N.Y.*, **24**, 1256.

Rosenbaum, J. (1941) *Arch. Ophthalm., N.Y.*, **25**, 477.

Stallard, H. B. (1940) *Brit. J. Ophthalm.*, **24**, 451.

LARYNX DISEASES

See also B.E.M.P., Vol. VII, p. 612; Cumulative Supplement, Key Nos. 918-927; and Surveys and Abstracts 1939, pp. 90 and 398; 1940, p. 375.

Acute Laryngitis

Treatment

Helium-oxygen.—G. Delfs states that helium-oxygen inhalation is an advance in the treatment of laryngitis and tracheitis. The mixture employed consists of 79 per cent of helium and 21 per cent of oxygen. The inhalation may be given in periods of 15 minutes to 1 hour, or longer, 3 to 6 times a day. The best apparatus for adults is the Benedict helmet type of hood; for older children oro-nasal masks may be employed.

Laryngo-tracheobronchitis

Chemotherapy.—R. R. MacGregor treated 9 cases of acute laryngo-tracheobronchitis with sulphanilamide, and 4 with sulphapyridine. The usual standard dosage was employed. Adjuvant measures consisted of blood transfusions on admission to hospital and maintaining the children in an atmosphere of great humidity. In some cases the oxygen tent was used. Of the 13 patients, 11 recovered; the 2 who died were moribund on admission to hospital.

D. Weisman and H. Russell treated 5 cases of acute staphylococcal laryngo-tracheobronchitis in infants, and 2 cases of staphylococcus bacteraemia in children, with sulphamethylthiazole. Employing dosages varying from 1½ grains (0.09 gramme) to 3 grains (0.19 gramme) per pound of body weight in 24 hours, a satisfactory and effective concentration of the drug in the blood was obtained. The clinical response to the treatment was striking, all the patients recovering.

Tumours of the Larynx

Clinical picture

Boeck's sarcoidosis.—D. L. Poe reports a case of sarcoidosis of the larynx in a woman 38 years old. The patient reported to the laryngological department because of hoarseness. Her face, nose, arms, and legs and the fingers of both hands showed the characteristic nodules and plaques of Boeck's sarcoidosis. Examination of the mouth, pharynx, larynx, and upper

part of the trachea showed infiltrations in the roof of the mouth, but nothing abnormal in the pharynx; there were nodules of various sizes on the epiglottis.

Operations

Anaesthesia

Malignant growths of larynx.—J. I. Kemler recommends a mixture of nitrogen monoxide and oxygen anaesthetic for operations on malignant growths of the larynx. The method is described as perfectly safe, does not irritate the lungs, and is free from side-effects. The patient is awake immediately after the operation. The mixture contains 85 per cent of nitrogen monoxide and 15 per cent of oxygen under a pressure of 5 to 10 millimetres. With this anaesthetic the patient can be kept in a somnolent condition throughout the operation without the production of cyanosis.

Delfs, G. (1941) *Arch. Dis. Childh.*, **16**, 52.

Kemler, J. I. (1941) *Arch. Otolaryng.*, *Chicago*, **33**, 707.

MacGregor, R. R. (1941) *Canad. med. Ass. J.*, **44**, 48.

Poe, D. L. (1940) *Arch. Otolaryng.*, *Chicago*, **32**, 315.

Weisman, D., and Russell, H. (1940) *J. Pediat.*, **17**, 31.

LEAD POISONING

See also B.E.M.P., Vol. VII, p. 658; Cumulative Supplement, Key No. 931; and Surveys and Abstracts 1939, p. 400; 1940, p. 376.

Aetiology

Lead hazards in printing

H. W. Ruf and E. L. Belknap, investigating the lead hazards in certain phases of printing, found that the amount of atmospheric lead present over the metal-pots of operating linotype, monotype, and Ludlow-type casting machines is not sufficient to necessitate the installation of ventilating equipment for its elimination. An examination of 40 printers from 14 different shops in which the average industrial hygienic measures were observed, showed that there was not any history of lead intoxication, though all but 30 per cent had more than 5 years' exposure, and 62 per cent were 30 years of age or older. None of the printers showed evidence of lead absorption as demonstrated by the lead line, and only 13 per cent showed non-persistent stipple cells of from 1 to 3 per 50 oil-immersion fields. Lead absorption was evidenced only by the detection of lead in the urine with an average excretion of 0.19 milligram per litre. The general health of the men was excellent.

Bullets lodged in the tissues

W. Machle reviews 40 reported cases of lead poisoning from bullets lodged in the tissues. Of these only 3 fulfilled all the modern criteria for a diagnosis of lead poisoning, and in 7 others the diagnosis appeared to be probable. Another 13 showed signs of lead absorption. The author reports 2 cases examined by him in which determination of concentrations of lead in the urine and blood demonstrated that lead absorption of a magnitude comparable to that met with in industry can result from embedded bullets. The possibility of delayed intoxication should have some weight in deciding whether or not to remove bullets.

Clinical Picture

Central nervous system

Encephalopathy in children.—A. J. Akelaitis states that the clinical picture of lead encephalopathy in children is analogous to those conditions in which the intracranial pressure is increased. The prognosis is grave, and sequels are frequent if the child survives the acute stages. The clinical picture in adults is analogous to that found in any severe intoxication involving the brain. The fundamental structural changes in the central nervous system are due to oedema, the exudate being probably blood serum. Other changes are endothelial hyperplasia in the smaller blood vessels and hyperplastic changes in the leptomeninges.

Encephalopathy simulating cerebral tumour.—A. M. Nussey and I. Drybrough-Smith report the case of a man, aged 41, with lead encephalopathy simulating cerebral tumour. On admission the patient was very restless and confused, and was vomiting continually. He was emaciated, and had a well-marked blue line on the gum margins. The case appeared to be one of lead encephalopathy, but, owing to the presence of left-sided weakness, ocular changes, and marked increase in the cerebrospinal fluid pressure, a growth in the brain had to be considered. Complete recovery followed expectant treatment.

Diagnosis

T. E. P. Gocher states that, when excretion of lead is observed in workers exposed to lead, a thorough study of the case should be made; all factors should be considered and compared to known lead symptoms. A high stippled cell count with or without a high reticulocyte count does not mean that lead toxæmia is present. Further, an increased excretion of lead in the urine does not prove that the case is one of lead poisoning. The higher the stippled count, the more toxic is the action of the lead.

Akelaitis, A. J. (1941) *J. nerv. ment. Dis.*, **93**, 313.

Gocher, T. E. P. (1940) *Northw. Med.*, *Seattle*, **39**, 291.

Machle, W. (1940) *J. Amer. med. Ass.*, **115**, 1536.

Nussey, A. M., and Drybrough-Smith, I. (1940) *Brit. med. J.*, **2**, 379.

Ruf, H. W., and Belknap, E. L. (1940) *J. industr. Hyg.*, **22**, 445.

LEPROSY

See also B.E.M.P., Vol. VII, p. 682; Cumulative Supplement, Key No. 935; and Surveys and Abstracts 1939, p. 401; 1940, p. 379.

Aetiology

Geographical incidence

In Great Britain.—L. Rogers, J. H. Cook, and E. Muir, at the request of the British Empire Leprosy Relief Association, publish the results of their investigation into the number of cases of leprosy seen during the last 30 years in Great Britain. A circular letter was sent to 50 dermatologists, and help was specially given by J. M. H. MacLeod. Out of 87 cases thus collected, all but 6 were seen in London; among 78 cases in which such information is available in 35 the disease was contracted in India, including Burma. In 4 only did the disease arise in Great Britain; one had a conjugal infection, and the other three were first seen when respectively 12, 15, and 18 years old, thus indicating infection at the early susceptible age. There was not any case of infection in the British Isles from a neural or from a tuberculoid case in which leprosy bacilli are very few and hard to find. The infective lepromatous patients, numbering 22, were found to be, with the exception of 4, in such satisfactory conditions as not to be a serious danger to the community.

Pathology and Bacteriology

Mixed types

Tuberculoid leprosy.—H. W. Wade of the Leonard Wood Laboratory, Cullion, Philippines, reviews the questions (1) of relapses in tuberculoid leprosy and (2) whether or not tuberculoid leprosy may pass into the lepromatous form. It is generally considered that the resistance of patients with tuberculoid leprosy is good and the prognosis particularly favourable; some cases subside permanently, but the belief that tuberculoid leprosy is so benign is probably largely based on the experience that these patients come under observation during what may be called the original phase of the process and, after responding well to treatment, pass out of sight leaving the impression that they are cured; this would explain why the question of relapse is seldom raised. In the Philippines relapses are not infrequent; in one small group of patients nearly half relapsed. The question whether or not the tuberculoid may pass into the serious lepromatous form has been much debated. After quoting the opinions of others, and his own observations, the author points out that there may be the paradoxical situation of a patient with lesions histologically lepromatous but clinically tuberculoid. It is concluded that the transformation of a tuberculoid into the lepromatous form is not effected easily, and that this diagnosis must be approached with caution.

Treatment

Curative

Basic principles.—E. Muir, in an account of the principles underlying the treatment of leprosy, lays stress on the great difference between the more severe lepromatous and the slighter forms, the latter being localized and often abortive. It has not been seriously suggested that, as in major and minor smallpox, this is due to two strains of the responsible micro-organism. The difference depends, at least in the first place, on the host's resistance, exerted by the tissue cells, variously called histiocytes, monocytes, or macrophages. There may be an intense mitotic reaction to the bacilli with high resistance and typical of neural leprosy; this destroys or inhibits the bacilli. On the other hand, with a mild reaction and a low resistance, the bacilli may multiply in the wandering tissue cells and thus be conveyed to other sites. In any well-established case of lepromatous leprosy treatment must aim at two objectives: (1) to strengthen and stimulate the cells to act more vigorously and (2) to break down the triple defence of the bacilli. Local applications to the skin, such as hydnocarpus oil intradermically, and caustics, stimulate the tissue cells. Iodide of potassium breaks down the defence mechanism of the bacilli, but its use has often been abandoned on account of its dangerous qualities; in some lepromatous cases even a fraction of a grain causes severe reactions. Massive dye treatment is inadvisable; extremely concentrated dye in the treatment of lepromatous leprosy acts as an irritating foreign body, and in doses sufficient to cause evacuation of a leproma may be very dangerous. With available treatment it is possible to control neural leprosy, if the diagnosis is made early. What is most needed is a method of activating the tissue cells of patients with early lepromatous leprosy.

Blood transfusion.—A. R. Davidson records the results of blood transfusion given to 7 leprosy patients at the Pretoria Leper Institution. This was undertaken in response to a petition from all the European patients there. The Rand Blood Transfusion Service gave the treatment. Six transfusions of 350–400 cubic centimetres were given to each patient at monthly intervals. Specific effects on leprosy were not anticipated from blood transfusion of strange blood, but it was hoped that it would either build up the patient's resistance or perhaps even stimulate the reticulo-endothelial system. It was not possible to obtain patients with arrested leprosy as donors; it was decided to attempt this if the first trial showed any promise. Nine months after starting the transfusion no improvement could be found. Six of the seven patients showed various degrees of cutaneous involvement. The seventh was a neural case of the

tuberculoid type which under routine anti-leprotic treatment would have a very good prognosis, whereas the 6 other cases would have a bad outlook.

Grasset's tubercle endotoxoid.—On the supposition that there may be a group antigen for the *Mycobacterium leprae* and the *Mycobacterium tuberculosis*, A. R. Davison treated 10 cases of leprosy at the Pretoria Leper Hospital for 6 months with subcutaneous injections bi-weekly of Grasset's tubercle endotoxoid, beginning with 0.05 cubic centimetre, and rising each week until 2.0 cubic centimetres were given at each injection. As improvement took place in all the neural cases of the tuberculoid type, the author concludes that Grasset's endotoxoid has some beneficial effect on tuberculoid lesions, and intends to continue work on cases of this type. Not any benefit was obtained in 4 cases of cutaneous leprosy.

Diphtheria formol toxoid.—A. R. Davison and E. Grasset report their results of an investigation upon the clinical and immunological effects of treatment with diphtheria formol toxoid, as employed in leprosy by D. R. Collier. Injections, beginning at 0.5, then 1 and then 2 cubic centimetres, were given every fortnight; if at this stage there was not any reaction the dose was raised by 1 cubic centimetre at each injection until 10 cubic centimetres were reached. The results were assessed 9 months after the treatment began. Of 100 lepers who started treatment, 72 completed it; of these 12 became worse, 34 did not show any appreciable change, 21 showed slight improvement, and 5, or 6.9 per cent, much improvement. This very slight therapeutic result as compared with those obtained by Collier is not explained. Collier believed that adrenal inadequacy was a necessary antecedent to leprosy, but in a review of 5,000 lepers not any case of gross adrenal inadequacy was recognized by the authors.

Lepromatous ulceration.—E. Muir from experience in India found that of the two forms of ulceration in leprosy—the lepromatous and the trophic—the latter was much the commoner. An investigation of all ulcers in the large leprosarium at Purulia showed only between 1 and 2 per cent to be bacteriologically positive, the rest being trophic in nature and due to involvement of the nerve supply. At the Trinidad leprosarium at Chacachacare, however, the great majority of ulcers were lepromatous, and due to breaking down of nodules and diffuse leproma; they are full of masses of leprosy bacilli which are constantly shed off from the surface. The treatment of these ulcers was a difficult problem, and occupied much time. Muir tried on these ulcers a method recommended by J. A. Ross and K. F. Hulbert for air battle burns, and obtained extremely good results; the treatment as adopted consisted of painting first with a 1 per cent solution of gentian or methyl violet in alcohol, then with a 10 per cent solution of silver nitrate in distilled water, and lastly with 15 per cent solution of tannic acid in water. On the first day this process is repeated 3 or 4 times, but usually after the first day one painting either with tannic acid alone or with the dye solution followed by tannic acid was sufficient.

Davison, A. R. (1941) *Leprosy Rev.*, 12, 18.

— (1941) *ibid.*, 13, 32.

— and Grasset, E. (1941) *Leprosy Rev.*, 12, 68.

Muir, E. (1940) *Leprosy Rev.*, 11, 162.

— (1941) *ibid.*, 12, 40.

Rogers, L., Cook, J. H., and Muir, E. (1940) *Leprosy Rev.*, 11, 170.

— — (1940) *Brit. med. J.*, 2, 7.

Ross, J. A., and Hulbert, K. F. (1940) *Brit. med. J.*, 2, 702.

Wade, H. W. (1941) *Leprosy Rev.*, 12, 3.

LEUCORRHOEA AND OTHER NON-HAEMORRHAGIC VAGINAL DISCHARGES

See also B.E.M.P., Vol. VII, p. 710; Cumulative Supplement, Key Nos. 937–939; and Surveys and Abstracts 1939, p. 403; 1940, pp. 19, 32, and 382.

Leucorrhoea

Clinical picture

Monilial vaginitis.—W. G. Liston and L. G. Cruickshank report on an investigation of 200 consecutive pregnant women attending the leucorrhoea clinic at the Royal Maternity Hospital, Edinburgh. Forty-nine, or 24.5 per cent, of these patients were found to have vaginal thrush, thus coming second to trichomoniasis (40 per cent) as the most frequent cause of leucorrhoea. This usually harmless infection may be communicated to the babies of affected mothers, more often multiparae than primiparae, and in some institutions gives rise to severe epidemics associated with a mortality not always recognized as thrush which may be ascribed to diarrhoea or broncho-pneumonia. The thrush fungus, though usually confined to the mouth, may extend to the oesophagus causing vomiting and diarrhoea, and to the bronchi causing broncho-pneumonia. In vaginal thrush the infection may exceptionally, in chronic cases, invade the cervix and uterus. In vaginal involvement the epithelial cells are usually well filled with glycogen and thus resemble those in films from normal pregnant women. The pH reaction of the vaginal contents depends largely on the glycogen content of the epithelial cells, and in turn the vaginal infection by different parasites, the thrush parasite thriving best on slightly acid media with a pH of about 5. Of the 49 patients with vaginal thrush 37 complained of a discharge, and 16 of irritation, which in 5 was so severe as to prevent sleep.

Attention is drawn to the confusion due to the multiple nomenclature of the thrush parasite from the original name *Oidium albicans* (Robin, 1847) to that of *Monilia albicans* (Zopf, 1890), the latter having become more usual now. The authors recommend the use of *Oidium albicans* for the parasite, and thrush for the disease, a qualifying adjective, such as oral or vaginal, being used to show the site.

Liston, W. G., and Cruickshank, L. G. (1940) *Edinb. med. J.*, N.S. (iv), 47, 369.

LEUKAEMIA

See also B.E.M.P., Vol. VIII, p. 1; Cumulative Supplement, Key Nos. 940-955; and Surveys and Abstracts 1939, p. 404; 1940, pp. 32 and 382.

The Leukaemias: All Types

Treatment

X-rays: 'spray' technique.—W. P. Murphy recommends that the treatment of chronic leukaemia should be so applied and regulated that the disease is kept constantly under control with avoidance of the severe relapses which so often occur. The method suggested is the frequent determination of the leucocyte level followed by X-ray exposures often enough to maintain the level as near normal as possible. X-ray therapy should be applied in small dosage by the 'spray' technique to avoid severe reactions. This method is claimed to have some advantage over the more generally used interval massive dose method in prolongation of life, and the general health and economic efficiency of patients.

Myelocytic Leukaemia

Chloroma

Clinical picture.—T. A. Kemp and E. R. Williams record as chloroma marked by nasal and vaginal haemorrhage the case of a girl, aged 1½ years at the date of onset, 9 months before death. The child was pale with sunken eyes and hollow cheeks, and did not show the 'chloromatous facies'. The temperature varied between 99° and 100.5° F., the total leucocyte count was 17,000, with 35 per cent myelocytes; a little later myeloblasts, 17 per cent, were found; the red cell count was 1,650,000, colour index 0.9, haemoglobin 30 per cent. Radiologically the femora, tibiae, and fibulae showed fairly regular periosteal new bone formation parallel to the cortex which showed some irregular destruction. Three weeks before death flaccid paralysis with incontinence of urine and faeces occurred. The blood picture and the radiological examination did not leave any doubt about the diagnosis; otherwise the history of epistaxis and vaginal haemorrhage might have suggested infantile scurvy. The necropsy showed that there was wide-spread epidural growth in the spinal canal and over the brain, but not in the cord or brain. Nervous symptoms have seldom been reported. There were 8 lumps over the right frontal and both parietal regions of the scalp, which were slightly blue during life. None of the tumour masses was green. The authors' summary of the subject contains the following points: chloroma is more than twice as common in children as in adults, and in males as in females; the largest number of cases occur at about the age of 5 years. The skull and orbital regions are especially involved and give rise to the 'chloromatous facies'. Two main clinical forms have been described (I. G. Jones, 1939): (1) usually seen in children and more rapidly fatal than the other; the chloromatous masses are more prominent than the anaemia, (2) usually in adults, the leukaemic signs are more in evidence than the chloromatous masses.

Chronic myeloid leukaemia

Leukaemoid.

—According to J. M. Hill and C. N. Duncan, the introduction of chemotherapeutic agents of the sulphonamide group has sufficiently increased the incidence of leukaemoid reactions to justify more general attention. The term leukaemoid was first used in 1926 for blood pictures resembling those of leukaemia by E. B. Krumbhaar who divided the cases into two main groups: (1) those presenting a real difficulty in the differential diagnosis from leukaemia, and (2) those resembling leukaemia in the blood picture only. A large number of conditions may thus imitate leukaemia; F. J. Heck and B. E. Hall in 1939 collected 16 clinical conditions which have been responsible for this type of blood picture. Hill and Duncan adopt the following criteria as characteristic of a myeloid leukaemoid reaction: (1) a total leucocyte count of more than 50,000, (2) the presence of immature cells of the 'blast' stage, or (3) a combination of (1) and (2), and also construct a classification of myeloid leukaemoid reactions under three main headings, each with many subdivisions giving the mechanism, the general features of the blood pictures and the diseases that may be responsible. The main divisions are: (1) irritation or stimulation of the bone marrow by physical, chemical, or allergic factors; this is the largest group, and includes bone metastases and infections; (2) liberation leucocytosis; the bone marrow responds to an overwhelming demand by acute haemolysis in sulphonamide poisoning and acute haemolytic anaemias, haemorrhage or septicæmia; (3) ectopic haematopoiesis, that of the formation of blood-producing foci outside of the bones and usually due to destruction or crowding of the bone marrow, as in osteosclerosis, tumours invading bone marrow, or lipid histiocytosis. The details of 9 cases illustrating the problems of these leukaemoid reactions are given. The differential diagnosis of leukaemia from the leukaemoid reaction may be very difficult, but the existence of a disease known to cause a leukaemoid reaction, for example, cancerous invasion or sepsis of bone marrow, is a practical point. The characters of the blood pictures are tabulated as follows:

Clinical picture

Involving the nail-bed.—G. M. Lewis and J. F. Ricchiuti report a case of lichen planus involving the nail-bed, in a man aged 33. Characteristic lesions had appeared on the legs and forearms and most of these disappeared spontaneously. Following this a violaceous papule appeared on the nail-bed of the left thumb, within the lunula. As the lesion grew, the nail-plate over it became thinned, and the portion, distal to the lesion, showed longitudinal striae. Several applications of X-rays cleared up the lesion.

Treatment

J. F. Burgess reports 15 cases of lichen planus treated by vitamin B complex. In acute cases the response was good, exerting almost, at times, a specific effect, but in chronic cases with much thickening of the skin improvement was much slower. Attempts to find out the possible value of the individual constituents of B complex did not succeed in showing any therapeutic specificity, and the use of the B complex is recommended.

Burgess, J. F. (1941) *Canad. med. Ass. J.*, **44**, 120.

Lewis, G. M., and Ricchiuti, J. F. (1940) *Arch. Derm. Syph., N.Y.*, **42**, 607.

Newman, A. H. (1941) *Canad. med. Ass. J.*, **44**, 175.

LIPOIDOSES, THE

See also B.E.M.P., Vol. VIII, p. 67; and Surveys and Abstracts 1939, p. 406.

Gaucher's Disease**Clinical picture**

Biopsy examination of pingueculae.—T. East and L. H. Savin report the case in a man, aged 59, of Gaucher's disease with involvement of the liver, the usual slight anaemia, and typical pingueculae. Histological examination of biopsy sections of the pingueculae showed beneath the epithelium small collections of large endothelial cells, the cytoplasm of which was degenerate and foamy in appearance. Frozen sections did not show any fat-staining particles.

Diagnosis

Sternal puncture.—J. N. M. Chalmers reports a case of Gaucher's disease in a boy 9 years old. The diagnosis was made by sternal puncture; examination of the material thus obtained showed a hyperactive cellular marrow with an increase of erythroblasts and normoblasts. Leucopoietic elements appeared to be reduced in number. Gaucher cells with typical reticulated cytoplasm and eccentric nuclei were seen. There was great clinical improvement after splenectomy.

Schüller-Christian Syndrome**Clinical picture**

M. Freund and M. L. Ripps report on a case of Schüller-Christian (Hand-Schüller-Christian) syndrome in a male infant. The most conspicuous manifestation of the disease was enlargement of the lymphatic glands which appeared at the age of 7 weeks. Characteristic osseous changes appeared at the age of 13 months. Biopsy of a lymphatic gland showed histiocytic granulation tissue without cholesterol, but at the necropsy characteristic lipid granulomas were found.

Involving middle ear and temporal bone.—H. Rosenwasser reports a case of lipid granulomatosis (Hand-Schüller-Christian syndrome) in a woman of 50, with diffuse involvement of the middle ear and temporal bone as the only manifestation of the disease. The clinical course, X-ray findings, and the results of pathological examination of material removed at operation suggested the diagnosis of carcinoma of the middle ear. Further examination of the microscopical sections, however, showed the true nature of the disease. X-ray therapy gave excellent results.

Differential Diagnosis**Xanthomatous biliary cirrhosis**

M. W. Comfort, V. D. Shepard, and A. M. Snell record the clinical picture of a widow, aged 52, with a history for 9 months of hepatic and splenic enlargement, jaundice, pruritus, xanthomatous patches in the creases of the hands and fingers, a pulsating telangioma on the right wrist, and hyperlipaemia, a prominent increase of cholesterol and lecithin, but without any increase in neutral fats. The ratio of cholesterol to cholesterol esters varied, sometimes being inverse, at other times direct. The case was distinguished from the ordinary biliary cirrhosis with high cholesterol values by the degree of hyperlipaemia and the presence of xanthomas. The clinical picture was that of xanthomatous biliary cirrhosis as described by Thannhauser, who regarded the jaundice as obstructive and due to xanthomatous lesions in the bile-ducts, thus agreeing with Hilton Fagge who described this in 1873. Other conditions somewhat resembling but differing from xanthomatous biliary cirrhosis are (1) the hepatosplenomegaly-lipoidosis of Bürger and Grutz which is characterized by the complete absence of jaundice; (2) in some cases of diabetes mellitus the liver is large and fatty, there is hyperlipaemia and xanthoma diabeticorum; and other examples of lipoidosis as in Gaucher's disease, Niemann-Pick disease, and the Hand-Schüller-Christian syndrome. In the case reported by Snell and his colleagues the patient was carefully dieted with a low allowance of cholesterol and fat, but the disease progressed.

Chalmers, J. N. M. (1940) *Arch. Dis. Childh.*, **15**, 230.

Comfort, M. W., Shepard, V. D., and Snell, A. M. (1941) *Proc. Mayo Clin.*, **16**, 374.

East, T., and Savin, L. H. (1940) *Brit. J. Ophthalm.*, **24**, 611.

Fagge, C. H. (1873) *Trans. Path. Soc. Lond.*, **24**, 242.

Freund, M., and Rippes, M. L. (1941) *Amer. J. Dis. Child.*, **61**, 759.

Rosenwasser, H. (1940) *Arch. Otolaryng.*, Chicago, **32**, 1045.

Thannhauser, S. J. (1940) *Lipidoses: Diseases of the Cellular Lipid Metabolism*, Oxford University Press, American Branch.

LIVER DISEASES: LIVER FUNCTION TESTS

See also B.E.M.P., Vol. VIII, p. 81; Cumulative Supplement, Key No. 976; Surveys and Abstracts 1939, p. 406; 1940, pp. 116 and 385; and p. 4 of this volume.

Tests

Comparative review

C. J. DeLor and H. L. Reinhart state that the hippuric acid, bromsulphthalein, serum bilirubin, blood prothrombin, and total blood cholesterol roughly parallel each other as hepatic function is diminished. The galactose tolerance test was the least reliable of the hepatic function tests used in their investigations. The bromsulphthalein test was the most sensitive test of this series for the identification of early liver damage. As estimated by these methods the mortality rises in cases with 50 per cent or more diminution of liver function.

Phenolphthalein.—B. Fantus, F. Steigmann, and J. M. Dyniewicz, investigating the effect on the liver of the ingestion of phenolphthalein in therapeutic doses, come to the following conclusions. There is not any evidence that the drug plays any part in the aetiology of jaundice, and its administration to 120 jaundiced patients did not interfere with recovery. Given to 425 non-jaundiced patients, it did not cause jaundice. Liver function tests in 12 patients with chronic constipation, taking 5 grains (0.3 gramme) of white or 2 grains (0.12 gramme) of yellow phenolphthalein daily, for months, showed no signs of liver damage. The authors find that the drug, in therapeutic doses, is not harmful to the liver.

Intrahepatic circulation of blood

Quartz-rod transillumination.—K. G. Wakim reports on observations made by means of quartz-rod transillumination adapted from Knisely's method, on the intrahepatic circulation of intact amphibians (frogs) and mammals (rats). In both animals the intrahepatic circulation shows intermittence, with phases of circulatory activity in the sinusoids alternating irregularly with phases of inactivity. During circulatory inactivity the sinusoids may either go through a storage phase during which they are packed full of blood cells, or a non-storage phase during which the sinusoids have scarcely any blood cells in their potential lumina. In ordinary conditions when the liver is not under the influence of either excitatory or inhibitory agents, the hepatic circulation possesses a high functional reserve, about 75 per cent, of the circulation within the various lobules. In both animals arterio-venous communications exist between branches of the hepatic artery and of the portal vein in the interlobular spaces. In the frog, but not in the rat, such arteriovenous anastomoses also occur between branches of the hepatic artery and of the hepatic veins. The hepatic artery supplies blood to the hepatic parenchyma through several routes. The administration of thyroxine, of glucose, or of particulate matter stimulates intrahepatic circulatory activity.

DeLor, C. J., and Reinhart, H. L. (1940) *Amer. J. clin. Path.*, **10**, 617.

Fantus, B., Steigmann, F., and Dyniewicz, J. M. (1941) *Amer. J. digest. Dis.*, **8**, 176.

Wakim, K. G. (1941) *Proc. Mayo Clin.*, **16**, 198.

LIVER DISEASES: BLOOD VESSELS

See also B.E.M.P., Vol. VIII, p. 87; and Cumulative Supplement, Key No. 970.

Portal Vein

Suppurative pylephlebitis

Thorium dioxide in diagnosis.—H. Koster emphasizes the value of thorium dioxide as a diagnostic aid in questionable cases of pylephlebitis, and as the determining factor in deciding upon abdominal or liver exploration. Although it is not absolutely certain that this contrast medium is entirely harmless, its great value as a differential diagnostic help in cases of suspected suppuration in the liver does not allow any anxiety about possible toxic reactions to contra-indicate its use.

Koster, H. (1940) *Radiology*, **35**, 728.

LIVER DISEASES: HEPATITIS, CHRONIC

See also B.E.M.P., Vol. VIII, p. 118; Cumulative Supplement, Key No. 974; and Surveys and Abstracts 1939, p. 409; 1940, pp. 28 and 387.

Clinical Picture and Clinical Types

Abdominal venous thrill

L. A. Wilson reports the case of a boy, aged 15 years, with cirrhosis of the liver. With the patient standing, several distended anastomotic veins were seen in the abdominal wall, chiefly above the umbilicus. A continuous thrill was felt directly below the umbilicus, and was

obliterated by light pressure in this area, and also when the patient stood up. There was also a continuous roaring murmur audible in the area of the thrill, and less loudly over the whole anterior abdomen. This murmur disappeared on deep pressure, and became louder and rougher on full inspiration. It was slightly diminished when the patient was standing.

Chronic hepatitis with predominant jaundice

Hanot's unilobular cirrhosis.—At a meeting of the Clinical Section of the Royal Society of Medicine, A. Abrahams showed a woman, aged 48, who for 10 years had periodically been jaundiced; in addition, the skin had been brown in the absence of jaundice. The liver and spleen, slightly enlarged at an early stage, were greatly enlarged. Parkes Weber thought that at the late stage the cirrhosis was no longer unilobular only. B. Pearson suggested that the condition was one of recurrent subacute yellow atrophy.

Relation between multiple neuritis and hepatic cirrhosis

Vitamin deficiency.—E. Wayburn and C. R. Guerard analyse the records of patients seen at the San Francisco hospital during the years July 1, 1928, to January 1, 1939, on the relation of multiple peripheral neuritis or, as Wechsler prefers to call it, peripheral neuropathy, to hepatic cirrhosis in the light of the now established causal relation of vitamin B deficiency to peripheral neuropathy. There were 273 patients with hepatic cirrhosis, care being taken to exclude fatty alcoholic livers with peripheral neuropathy. The criteria for the diagnosis of peripheral neuropathy were a history of pain, burning, numbness or weakness in the limbs, paraesthesia, tenderness of the calves, paresis, paralysis and atrophy of muscles, and alteration of the patellar and ankle jerks. No one test was regarded as diagnostic. Men were more frequent than women in the ratio of about 6 to 4. In four-fifths of the patients the condition was regarded as far advanced or moderately advanced; gastro-intestinal haemorrhage had occurred in a third, and there was a history of alcoholism in more than 70 per cent, and of pellagra in 3 per cent. Peripheral neuropathy occurred in 17 per cent and among these the sex ratio was reversed, 64 per cent being females, whereas cirrhosis alone was commoner in males. It is becoming increasingly clear that vitamin deficiencies rarely occur singly. Alcoholism, general dietary deficiency, and deficiency of thiamin intake were associated with both diseases. The peripheral neuropathy of the cirrhotic patient regressed when high vitamin treatment and particularly large amounts of vitamin B were given.

Abrahams, A. (1941) *Proc. R. Soc. Med.*, **34**, 321.

Pearson, B. (1941) *Proc. R. Soc. Med.*, **34**, 322.

Wayburn, E., and Geurard, C. R. (1940) *Arch. intern. Med.*, **66**, 161.

Weber, P. (1941) *Proc. R. Soc. Med.*, **34**, 322.

Wilson, L. A. (1940) *Lancet*, **2**, 745.

LIVER DISEASES: TUMOURS

See also B.E.M.P., Vol. VIII, p. 151; and Surveys and Abstracts 1940, p. 388.

Malignant Tumours

Primary tumours

Racial incidence.—C. Berman analyses the incidence of 270 cases of primary carcinoma of the liver in the Bantus in and around Johannesburg, Transvaal, in the nine years 1925–33. Review of the literature of this form of carcinoma shows that it is very rare among white-skinned races—the necropsy rate being 0.13 per cent in Europe, and 0.25 per cent in America. On the other hand it is common among all dark-skinned and yellow-skinned races, especially the Japanese, and in some races is 40 times that in Europe. Among Europeans in Johannesburg it is very rare, and corresponds with that of white races in other parts of the world. It is a racial rather than an environmental disease. Among the Bantus it is predominantly one of young males, 32.6 per cent being under the age of 40; among 229 in miners, all males, 90 per cent of all cases of carcinoma were primary in the liver. This paper contains much statistical information based on necropsies. In a subsequent article the clinical features of the disease as seen among the Bantus in the Transvaal are described by C. Berman on the basis of an analysis of 66 cases. Five clinical groups are given, the first of which is typical, the others being atypical. (1) 'Frank' carcinomas; these constitute 42, or 63.6 per cent, of the total. The onset was gradual, and the symptoms were abdominal pain in 90 per cent, asthenia in 8.6 per cent, loss of weight and emaciation in 81 per cent, ascites in 55 per cent, jaundice in 43 per cent, and fever in 38 per cent. The liver was enlarged in all cases and tender in 90 per cent. (2) 'Acute abdominals'; these consist of 6 cases of latent primary carcinoma which suddenly showed acute surgical conditions of the abdomen, caused by rupture of malignant nodules or erosion of blood vessels on the surface of the liver, causing intra-peritoneal haemorrhage, and rendering diagnosis difficult. (3) 'Febrile' cases (5 cases) show rapid growth of the liver with symptoms resembling those of amoebic abscess. (4) 'Occult' cases (10 cases) are of latent hepatic growth in patients with symptoms other than those of hepatic disease, and found in the course of routine examination or at necropsy; and (5) 'Metastatic' cases; 3 cases in which there were secondary growths in the lungs, ribs, and brain.

Morbid anatomy.—In a pathological analysis C. Berman follows up his clinical account. It is first pointed out that the weight of the normal Bantu liver is as a rule about 9 ounces (250 grammes) heavier than the normal European liver. Among 42 cases of primary carcinomas of the liver the weight of the liver averaged about 8½ pounds (3,925 grammes) with

extremes of 15½ pounds (7,100 grammes) and 4 pounds (1,900 grammes). Macroscopically the cases fell roughly into multiple discrete nodules (34 cases) and a single massive growth in 20 cases; but the nodules may run into a confluent mass. Histologically the growths were derived from the polygonal cells of the liver, or hepato-cellular (24 cases), and in 1 case from the cells of the small bile-ducts (cholangio-cellular). Cirrhosis of the liver was always present. Extra-hepatic metastases were found in 31, or 57·4 per cent, of the cases, and of these 27, or 89 per cent, were in the lungs, in 25 cases in both lungs. On the debated question of whether primary carcinoma of the liver is unicentric or multicentric in origin the author concludes that it is, from both macroscopic and microscopic evidence, unicentric in origin.

Berman, C. (1940) *S. Afr. J. med. Sci.*, **5**, 54 and 92.

— (1941) *ibid.*, **6**, 11.

LUNG DISEASES: ATELECTASIS AND COLLAPSE

See also B.E.M.P., Vol. VIII, p. 160; Cumulative Supplement, Key No. 985; Surveys and Abstracts 1940, p. 388; and p. 77 of this volume.

Aetiology

Pneumothorax

Embolism.—J. H. Marks reports 2 proved cases of pneumothorax due to pulmonary infarction. Since pulmonary infarction is secondary to a morbid process elsewhere in the body, a pneumothorax in a patient known to be the subject of a disease likely to cause embolism should be considered as a possible cause of the pneumothorax. The possibility becomes a probability if an area of consolidation is present at or near the base of the lung, and especially if there is an inflammatory process elsewhere in the body. X-ray examination greatly assists the diagnosis.

Clinical Picture

In the new-born

S. H. Snider reports a case of massive unilateral atelectasis in a new-born baby. Three days after birth the nurse found a clot of blood about 0·5 by 2 centimetres in the bed. A radiogram of the chest taken immediately showed diffuse opacity of the left lung with some narrowing of the intercostal spaces on that side, and some shifting of the heart toward the left. Another radiogram taken some hours later showed complete disappearance of the opacity on the left side, the heart in its normal position, and no narrowing of the intercostal spaces on the left side. The diagnosis was massive atelectasis due to plugging of the left main bronchus with a blood clot, the atelectasis having rapidly cleared up on expulsion of the clot.

Marks, J. H. (1940) *New Engl. J. Med.*, **223**, 934.

Snider, S. H. (1941) *Med. Times, N.Y.*, **69**, 163.

LUNG DISEASES: ABSCESS AND GANGRENE

See also B.E.M.P., Vol. VIII, p. 172; Cumulative Supplement, Key No. 987; Surveys and Abstracts 1939, p. 410; 1940, p. 389; and p. 76 of this volume.

Pathology and Morbid Anatomy

Classification

R. H. Overholt and W. R. Rumel criticize the separation of pulmonary abscesses into acute and chronic stages, and suggest the adoption of a classification based on pathology. The separation of such abscesses into their simple and complicated stages is proposed. The simple stage includes a single or a multilocular cavity without secondary bronchiectasis. Complicated abscesses consist of multiple isolated daughter abscesses which are located in the surrounding zone of pneumonitis, and which do not connect with the primary cavity, and do not point on the surface of the lobe. In this group also are included patients who have acquired an associated bronchiectasis or empyema.

Treatment

Non-operative

Sulphonamide compounds.—J. S. Richardson reports a case of acute lung abscess in a man, aged 26, who was successfully treated with sulphapyridine. An X-ray photograph showed a thin-walled abscess at the apex of the right lung, well above the clavicle. The patient was given sulphapyridine, in a total dosage of 18 grammes (270 grains) during 3 days; he was then given sulphanilamide up to a total of 11 grammes (165 grains). The abscess and the surrounding area of inflammation disappeared entirely within 13 days.

G. F. Taylor, M. Yusuf, and N. L. Chitkara obtained striking improvement in 3 out of 7 cases of lung abscess from the use of sulphapyridine. None of these cases followed operations on the upper respiratory passages, but 3 occurred after lobar pneumonia. Five patients were given the drug orally, in doses of 2 grammes (30 grains) on admission to hospital, 2 grammes after 4 hours, then 1 gramme (15 grains) every 4 hours. In 4 of these cases vomiting began after a few hours, and treatment had to be stopped; the other patient made a rapid recovery. In 2 other cases soluble sulphapyridine was given in a dose of 1 gramme 3 times daily, by injection, for 7 days. In both cases there was a striking improvement, in one within 24 hours after the first injection, and recovery resulted.

Operative

Bronchoscopic treatment.—M. F. Arbuckle reports on the use of bronchoscopic treatment of

43 cases of lung abscess. This treatment consists of destruction of granulation tissue by the use of forceps and curettes, removal by suction of the contents of the abscess by special tubes made for this purpose and introduced directly into the cavity, and the instillation of guaiacol with 1 per cent of oil of sweet almonds, or lipiodol. The patients treated included those with acute, subacute, and chronic lung abscesses, with a duration of 2 weeks to 3½ years. The ages ranged from 3½ to 65 years. Of the 43 patients, 20 failed to recover or to show satisfactory improvement by bronchoscopy alone. Of the other 23 patients, 19 made complete recoveries, and 4 showed very satisfactory improvement.

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LUNG DISEASES: TUBERCULOSIS

See also B.E.M.P., Vol. VIII, p. 182; Cumulative Supplement, Key No. 988; Surveys and Abstracts 1939, pp. 114 and 411; 1940, pp. 94 and 389; and pp. 4, 75, and 77 of this volume.

Aetiology

Adverse tendency in mortality rate

Social survey.—G. P. Wright and P. D. Hart, in a discussion of the retardation in the decline in tuberculosis, consider that at least three important social changes are responsible, two of them affecting all members of the community indiscriminately and one affecting young women specifically. These are, a prolonged check to the rise in the standard of living, a slowing down in the reduction of overcrowding, and an increase in the proportion of women employed. The sharp rise in the birth rate in 1919–22 does not appear to be a causal factor. Because of war conditions the authors fear that there will be an adverse tendency in the mortality rate of pulmonary tuberculosis in the near future.

Morbid Anatomy and Pathology

Cardiac lesions

Chronic cor pulmonale.—L. V. Ackerman and K. Kasuga report on the incidence of chronic cor pulmonale, or hypertrophy of the right side of the heart, with or without cardiac failure, in 330 necropsies of pulmonary tuberculosis recorded between 1933 and 1940 at the San Francisco City and County Hospital. Patients under the age of 16 years and those with a minimal tuberculosis and dying in the general medical wards were not included. There was an incidence of 53, 16 per cent, examples of chronic cor pulmonale. Of the 53 cases 12 showed intrinsic cardiac disease of the endocardium or myocardium and were therefore excluded. The authors consider that pleuritic thickening plays but an unimportant part in obstruction of the pulmonary blood flow except when the adhesions are particularly excessive and of long standing as in an empyema. The 41 cases, which were quite free from gross or histological lesions of the heart and pericardium, were divided into (1) 21 with cardiac failure, (a) those with minimal usually terminal failure and (b) those (2 only) in which right-sided failure was the predominating feature; and (2) the 20 cases without any cardiac failure. In the 19 cases of cardiac failure severe anthraco-silicosis was present in 4, and in 14 there were chronic productive lesions of long duration with secondary emphysema and obliteration of the intercostal spaces. In uncomplicated pulmonary tuberculosis right-sided cardiac hypertrophy is infrequent; right-sided hypertrophy without heart failure occurs in about 6 per cent of all patients dying from pulmonary tuberculosis. Pneumothorax of long duration with much collapse and thickened pleura is sometimes responsible for right-sided hypertrophy. When cardiac and pulmonary disease combine to cause pulmonary hypertension the changes in the pulmonary arterial tree are usually degenerative rather than hyperplastic.

In the introduction to this article reference is made to acute cor pulmonale which when not due to disease of the left side of the heart is most often caused by a large pulmonary embolus, dilatation of the pulmonary artery and conus being demonstrable radiologically or by physical signs. Whether subacute cor pulmonale should be recognized is left open. Brill and Robertson used the term to describe blocking of the lymphatics of the lung by carcinomatous metastases, a condition previously described by Barnes, Thomson, and Lamb as due to a myosarcoma in the recto-genital pouch and causing intense erythraemia.

Clinical Picture

Pleuritic effusion

Eosinophilia.—A. M. Gill reports a case of tuberculous pleuritic effusion, in a male of 19, in whom a blood count showed a total of 9,200 leucocytes per cubic centimetre, with 14 per cent of eosinophils. Fluid withdrawn from the chest was turbid, slightly blood-stained, and in a differential count showed the remarkable figure of 80 per cent of eosinophil polymorphonuclear leucocytes. The clinical diagnosis of tuberculosis, on which doubt had been thrown by the unexpected laboratory finding of eosinophilia, was confirmed by biopsy and necropsy. The author emphasizes the persistence of the blood eosinophilia in a patient whose general condition was steadily deteriorating.

Course and Prognosis

Gastro-intestinal complications

L. L. Hardt and S. J. Cohen discuss the gastro-intestinal complications of pulmonary tuberculosis, and state that in a series of 1,000 cases tuberculous enteritis was diagnosed in 78.3 per cent, and that in 1,000 selected necropsies of patients who had died of pulmonary tuberculosis it was found in 71 per cent. The incidence of peptic ulcer was slightly higher than in non-tuberculous patients and that of cholecystitis and cholelithiasis was about the same as in other groups of similar ages. In about 33 per cent of the cases amyloid disease of the liver and spleen was found. Chronic gastritis, especially chronic atrophic gastritis, was often present.

Post-operative complication

H. E. Pugsley and G. D. Richardson state that the most frequent serious post-operative complication in pulmonary tuberculosis is an extension of the disease in the lung. Patients in a condition of shock run an increased risk of the spread of the pulmonary lesion. On the other hand, patients with pulmonary disease in the chronic fibrotic phase generally tolerate anaesthesia and operation well. Those in the acute exudative phase are much more prone to develop a post-operative spread.

Diagnosis and Differential Diagnosis

Sputum examination

W. H. Roper and W. H. Ordway state that by the addition of gastric lavage for patients who require examinations of sputum, positive recovery of tubercle bacilli was increased from 34.8 per cent to 69.1 per cent in 123 newly admitted tuberculous patients. Gastric lavage is extremely valuable in those patients who do not expectorate or who produce unsatisfactory or negative sputum. The test is of assistance not only in the diagnosis but also in the management of the tuberculous patient. After years of treatment the sputum may disappear or become negative while the gastric contents still show the presence of virulent tubercle bacilli. A single negative gastric lavage does not exclude active tuberculosis.

Mantoux test

B. A. Dormer and J. Friedlander compare the Mantoux test and the tuberculin patch test in 200 children and find a high degree of correlation between the two tests. They conclude that, for mass surveys, the Mantoux test is undoubtedly the method of choice, advantages being the ease of application, the high degree of accuracy, and the absence of trauma.

X-rays

G. Jessel discusses the part played by mass radiography in tuberculosis, and maintains that fluoroscopy, though the cheapest method, has the disadvantage that it does not provide a permanent record. Miniature screen photography on the other hand, for use on a large scale, requires special apparatus and most careful organization. Miniature mass photography under favourable conditions provides a rapid method of weeding out those who present abnormal radiographic appearances, and these should be referred to a tuberculosis dispensary for detailed investigation. The re-examination of those classed as healthy should be undertaken periodically, especially in the so-called 'dangerous' industries.

Treatment

Social administration and colonization

Difficulties of temperament.—R. C. Wingfield emphasizes the importance of regarding the treatment of pulmonary tuberculosis as a whole, continuous and complete process, and condemns the term 'after-cure'. After years of experience Wingfield strongly supports the therapeutic programme advocated more than half a century ago by the late R. Philip, and shows the importance of the 'social' administration as well as of the clinical side of treatment. In the present administration the 'social' side is neglected and inefficiently carried out. The admitted want of success has aroused many attempts at rectification. The method of supplying special protected working and living conditions for the tuberculous by a number of schemes, exemplified by Papworth, would seem at first sight the logical answer to the difficulty, but they only touch the fringe of the problem. Why is this so? It is because the English working-class patient will not colonize. For 20 years Wingfield has been trying to persuade suitable patients to make use of the protection and the chance of life that such institutions offer. Only patients of a certain temperament, and then only when they have their backs to the wall, will ever accept, and then usually grudgingly. The idea of permanent regimentation in any degree is abhorrent, and with full knowledge of their position they will risk death to avoid it. This may be misguided, but it is an ingrained point of view that rules out protection by the colony system as an answer to the problem. It might be the correct answer in a totalitarian state, and therefore its failure in England may be a cause of congratulation.

Cure

By hemi-diaphragmatic paralysis.—A. Hope Gosse and M. R. Pollock report on the experience, recently much more extensive, of phrenic paralysis (primary evulsion or crush) in pulmonary tuberculosis. For 3 years primary phrenic evulsion, instead of artificial pneumothorax, has been adopted as the treatment for early, or moderately early, unilateral cases. A careful watch was kept for any disadvantage caused by phrenic paralysis in 39 patients who were thus treated alone or in combination with or without rest induced by artificial pneumothorax or other means. No example of ill effect was found, but cases that proved to be unsatisfactory

are frankly recorded. Sometimes the operation must be repeated; diaphragmatic paralysis thus induced varies considerably in duration, and may be due to differences in the crushing technique. When a second operation was necessary, evulsion was more often employed if the first had been a crushing procedure. It is concluded that phrenic paralysis and artificial pneumothorax are the two best methods of collapsing a tuberculous cavity; they should be regarded as at least of equal value. Phrenic paralysis should be promoted to the position of first choice; when successful, as it often is, the avoidance of years of refills with their complications gives phrenic paralysis the advantage.

By paraffin pack.—The use of a paraffin pack in 45 cases of apicolysis is further described by F. Ottaviano. Of the 45 patients, 13 had had previous thoracoplastic treatment. Of these 1 died, 6 were discharged as satisfactory with negative sputum and are able to work, 2 are continuing the cure at home, their sputa being positive, and 4 are still in hospital. Thirty-two had not had any previous thoracoplastic treatment; of these 5 died, 23 were discharged as satisfactory, and 4 are still in hospital. Only two of the five deaths were from a cause even remotely connected with the paraffin procedure, one from massive hydrothorax and one from pulmonary embolism. The pack was removed in 5 cases, this not necessarily indicating failure, since the sputum was negative. Paraffin was coughed up by 4 patients out of 45. This and perforation in cases of previous thoracoplasties are the main difficulties. On the other hand, results compare well with other treatment, especially for patients who are poor subjects for thoracoplasties. Unusual success is recorded in two cases of bilateral packing.

Artificial pneumothorax

Results and complications.—S. Diamond and H. T. Ivey report on the results and complications of pneumothorax therapy in 431 patients over 40 years of age. The method was successful in 20.2 per cent of the cases. The incidence of complications was no higher than that generally observed in younger patients. It may be necessary to continue a pneumothorax of doubtful efficacy slightly longer in patients in the fifth decade than would be advisable in younger patients.

Insulin and high carbohydrate dietary

G. Day reports the results obtained from feeding patients with pulmonary tuberculosis on a high carbohydrate diet and rendering their blood-sugar low by repeated hyper-insulation. The technique is as follows: the patient receives, during the 24 hours, 5 injections of insulin, each of 10 to 15 units; 3 of these are given half an hour before the chief meals—breakfast, lunch, and dinner. The others are given in the middle of the morning and the middle of the afternoon respectively, and are accompanied by a fruit drink containing 3 ounces of cane or grape sugar. To change an ordinary standard dietary into a high-carbohydrate low-fat dietary, at breakfast, porridge or cereals with plenty of toast and marmalade are taken; at lunch and dinner, soups are thickened with flour, puddings with a high carbohydrate content are prescribed, and the patient is encouraged to round off these meals with cheese and biscuits. The patient has a fruit drink at his bedside to ward off any untimely attack of hypoglycaemia. If ambulant he carries barley-sugar or sweets in his pocket. As the patient's blood-sugar is lowered during the half-hour before meals, he develops an appetite. Treated patients were found to gain, during the first seven months, on an average 3.86 pounds per month, as compared with 1.3 pounds in controls on an ordinary sanatorium dietary. This treatment has been employed on patients during 3 years; but the patients soon tire of the injections, and of 27 patients there were only 5 persisting in the treatment after 7 months. Analysis of the results compared favourably as regards increase of weight and the blood sedimentation index with controls. The manifestations of induced hypoglycaemia varied in different patients. The only other untoward incident was that in some patients the skin became sensitized to insulin injections; transient urticaria occurred, first at the site of subsequent injections and later at the site of all previous injections.

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Roper, W. H., and Ordway, W. H. (1941) *Amer. Rev. Tuberc.*, **43**, 543.

Wingfield, R. C. (1940) *Brompton Hosp. Rep.*, **9**, 158.

Wright, G. P., and Hart, P. D. (1941) *Amer. Rev. Tuberc.*, **43**, 357.

LUNG DISEASES: FIBROSIS

See also B.E.M.P., Vol. VIII, p. 215; and Cumulative Supplement, Key No. 991.

Diagnosis and Differential Diagnosis*A symptom of unilateral disease*

L. Hess states that in many cases of chronic affections of the lung, pleura, and mediastinum, basal pleuritic adhesions, chronic pneumonias, affections of the hilum lymphatic glands, and tumours of the bronchi, he has often seen the following sign. Whereas in cerebral hemiplegias the protruded tongue deviates toward the opposite or paralysed side, e.g. in a lesion of the left cerebral hemisphere the right half of the body is paralysed, with deviation of the tip of the tongue to the right, in affections of one side of the lung or of the mediastinum the tip of the tongue deviates to the affected side. The half of the tongue corresponding to the affected side is smaller than the other half. There is sometimes a slight fibrillary twitching of the muscle fibres, and the border of the tongue may be shallower on the deviated side. A sensory defect cannot be detected in either the anterior or the posterior part of the tongue.

Hess, L. (1940) *New Engl. J. Med.*, **223**, 417.

LUNG DISEASES: TUMOURS

See also B.E.M.P., Vol. VIII, p. 224; Cumulative Supplement, Key Nos. 992-994; Surveys and Abstracts 1939, pp. 115 and 415; 1940, p. 394; and p. 77 of this volume.

Malignant Tumours of Lungs and Bronchi*Primary*

Bronchogenic carcinoma.—R. G. Bloch and G. Bogardus analysed 88 cases of primary carcinoma of the lung. The youngest patient was 32, the oldest 82 years old, and 71.5 per cent occurred between the ages of 40 and 60. Loss of weight occurred in 59 but it is pointed out that a considerable loss of weight, such as 20 pounds, signifies the presence of abdominal metastases; the lung tumour alone has not been found to cause much loss of weight unless abscess formation has set in. Loss of weight to some degree occurred in 59 of the 88 cases. The analysis bears on the question whether or not irradiation, and especially in a more extensive degree, should unhesitatingly be given to every case because no serious ill effects occur. With this dictum the authors disagree. Their figures show that in the various age groups the duration of the life after the onset of symptoms in the patients treated radiologically and those not so treated was practically the same and that irradiation as a curative measure was a complete failure, as the mortality was not diminished and the duration of life not prolonged. It is pointed out that the patient with a hopeless pulmonary neoplasm dies an easier death without radiological treatment and that 'irradiation for psychological reasons is not in order'. The authors quote and confirm E. A. Graham's condemnation of irradiation treatment of primary carcinoma of the lung or bronchus. P. E. Steiner in his study of 21 cases of primary carcinoma of the lung found that doses of 5,000 roentgens did not destroy the carcinomatous cells as judged by the histological appearances. Comparison of periods of survival from the date of onset of symptoms in the 21 irradiated cases, and in 53 control cases that had not been irradiated, showed that irradiation did not notably prolong survival.

Malignant Tumours of Lungs and Bronchi*Cardiac metastases*

J. R. Reuling and L. Razinsky report a case of primary squamous-celled carcinoma of the bronchus of the upper lobe of the left lung with multiple cardiac metastases in a man aged 63. Necropsy showed that the growth had broken down into a cavity in the left upper lobe. The whole of the bundle of His was destroyed by the metastases. The case was of interest for several reasons. It presented nearly all the more usual cardiac abnormalities of neoplastic involvement of the heart. Thus, the onset of cardiac symptoms was marked by paroxysmal auricular fibrillation, followed by left bundle-branch block and, finally, by complete A-V dissociation with an Adams-Stokes syndrome.

Secondary

'Sulcus tumour' of the lung.—L. J. Breslin reports briefly under the title 'sulcus tumour' a carcinoma of the lung in the case of a man, aged 66 years, with radiological evidence of opacity at the apex of the left lung; later pain began in the left scapular region, which was at first paroxysmal but became continuous and so excruciating that he was anxious to undergo an exploratory operation and if possible section of the spinal nerve roots. Complete Horner's syndrome appeared on the left side. A diagnosis of superior pulmonary sulcus tumour had been made. Exploratory operation showed a hard tumour at the apex of the left lung, adherent to the pleura, and pressing upon and distorting the brachial plexus. Microscopically the tumour was an anaplastic carcinoma. Death from pneumonia and cardiac failure occurred on the fourth day after the operation. This syndrome was described in 1924 by Pancoast as radiologically showing evidence of a dense tumour at the extreme apex of one lung with erosion of one or more upper ribs, usually close to their vertebral attachment. He considered that the growth arose from the epithelium of one of the lower branchial clefts, and not from the lungs, pleurae, ribs, or mediastinum. But it is now thought that the complete clinical picture can be produced by any inflammatory or tumour mass, either primary or secondary.

Non-Malignant Intra-Thoracic Tumours*Clinical picture*

Chondroma of the bronchus.—M. Davidson records the rare condition of a pure cartilaginous tumour arising from a large bronchus. A man, aged 66, with paroxysmal cough and dyspnoea

so severe that for three years he had not been able to work, showed radiologically complete block of the main bronchus to the right lower lobe. Bronchoscopic examination proved the presence of a smooth, pinkish, rounded pedunculated tumour with a convex surface, which might have been an adenoma, and part of it was removed. Three days later a piece of tough white growth, histologically of pure cartilage, and about twice the size of a cherry stone, was expelled by violent coughing. Subsequently the remainder of the chondroma was removed bronchoscopically, and the relief from the cough was most satisfactory. The bronchi in the right lower lobe showed dilatation. Benign cartilaginous tumours of the lungs are recognized, but the author failed to find a case similar to this among the notes at the Brompton Hospital.

Bronchial sarcoidosis.—E. B. Benedict and B. Castleman record what appears to be the first case in which diagnosis of undoubted involvement of the bronchial mucosa by sarcoidosis was made by bronchoscopy. The patient was a negress, aged 20 years, with generalized sarcoidosis, especially in the cervical, pre-auricular, and submental regions in the lymphatic glands. The symptoms were those of partial obstruction of the trachea or bronchi, and clinically resembled those of asthma. Bronchoscopy showed redness and oedema with bleb-like formations throughout the bronchial tree; several biopsy specimens taken by the bronchoscope showed histological appearances consistent with the diagnosis, which was confirmed by a biopsy of a lymphatic gland in the neck.

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Graham, E. A. (1936) *Ann. Surg.*, **103**, 1.

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Steiner, P. E. (1940) *Arch. intern. Med.*, **66**, 140.

LUNG DISEASES: POST-OPERATIVE COMPLICATIONS

See also B.E.M.P., Vol. VIII, p. 235; Surveys and Abstracts 1939, p. 417; 1940, pp. 108 and 394; and pp. 12 and 71 of this volume.

Pulmonary Embolism

Aetiology

Incidence and occurrence.—N. W. Barker, K. K. Nygaard, W. Walters, and J. T. Priestley begin a series of statistical articles on the post-operative incidence of venous thrombosis and pulmonary embolism among 172,888 operations during 13 years at the Mayo Clinic. The data include cases with a clinical diagnosis of thrombophlebitis or of pulmonary embolism; cases of fatal pulmonary embolism, in 84 per cent of which the clinical diagnosis was confirmed or established by necropsy, and cases in which non-fatal pulmonary embolism or ante-mortem thrombosis or thrombophlebitis was discovered only at necropsy. The total of these cases of thrombosis with or without pulmonary embolism and of pulmonary embolism with or without evidence of other thrombosis was 1,665, or 0.96 per cent of all the patients operated upon. The incidence of these complications after various kinds of operations was investigated; among 21,366 thyroidectomies there were 24, or 0.11 per cent; among 13,103 operations on the biliary tract there were 230, or 1.76 per cent; and of 321 splenectomies there were 20, or 5.1 per cent. Laparotomies on the female pelvic organs involving ligature or injury of branches of the iliac veins; simple exploratory laparotomies on patients with inoperable malignant or inflammatory lesions, and prolonged operations with much damage to tissues favour thrombophlebitis. The incidence of venous thrombosis and pulmonary embolism is approximately twice as high in cases of repair of bilateral femoral or inguinal hernia as in cases of unilateral femoral or inguinal hernia; here the difference is only in the magnitude and duration of the operations.

In a further paper the authors analyse the 1,665 cases of post-operative venous thrombosis and pulmonary embolism with special reference to the time of occurrences during the post-operative period. Venous thrombosis occurred in 1,260 cases and of these 938 were clinically diagnosed as thrombophlebitis, in some 95 of which there were 2 or more episodes of thrombophlebitis, the first being counted as determining the onset. Cases occurred as early as the second post-operative day, as late as the hundred and fifteenth day, and the mean was the twelfth day. The complication occurred during the first 8 days in approximately a fourth of the cases, from the ninth to the fourteenth day inclusive in about half the cases, and after the fourteenth day in a quarter of the cases. There were 897 cases of pulmonary embolism, of which 343 were fatal; of these the fatal embolism was the first in 219, or 24 per cent. Of the 897 cases of embolism, both fatal and non-fatal, a non-fatal or only embolism was the first in 678, or 75.6 per cent, of the cases. The following deductions were regarded as probable: if an operated patient has a non-fatal embolism, he has slightly less than a one in five chance of a subsequent fatal pulmonary embolism, about three chances in ten of a subsequent embolism, fatal or non-fatal, and slightly less than one chance in two of some sort of subsequent thrombotic or embolic episode.

Predisposing conditions.—Among the 1,665 consecutive cases of venous thrombosis and pulmonary embolism, following 172,888 operations at the Mayo Clinic, the relative incidence of all the 1,665 cases was somewhat higher in females than in males; and this was particularly true of cases clinically diagnosed as thrombophlebitis, in which the ratio was approximately

three to two. The incidence of pulmonary embolism, both fatal and not lethal, was slightly higher in males. The youngest patient was 10 years of age, and the earliest age of fatal pulmonary embolism was 20 years. The most advanced age at which these post-operative complications occurred was 88 years; they are quite rare under the age of 20 years, and their incidence is definitely greater after the age of 50, especially in intestinal operations and hysterectomies. More than half the male cases occur between the ages of 50 and 69 years, and more than 60 per cent of the female cases between 40 and 59 years of age. The possible disposing conditions are cardiac diseases of various kinds, varicose veins, diseases of the blood-forming organs, especially secondary and hypochromic anaemias, and leukaemia and erythraemia; this last group was the most important numerically. Other possible disposing factors are obesity, cancer, and severe infections. From these statistics the risks of operations can be estimated; for example, a patient about to undergo abdominal hysterectomy who had none of these disposing factors would have a 2 per cent chance of the development of post-operative venous thrombosis with or without pulmonary embolism; whereas in a definitely anaemic patient the risk would be 9.3 per cent. But as in approximately a third of the 1,665 cases none of the possibly predisposing factors was established, the authors agree that these factors were not more than coincidental.

Diagnosis

Multiple chest-lead cardiograms.—P. Wood, writing on the differential diagnosis of pulmonary embolism from posterior myocardial infarction by electrocardiography, describes a new method of more accurate diagnosis from pulmonary embolism, and bases this on his observations and records of cases. He concludes that, although it may be difficult to distinguish acute pulmonary embolism from posterior myocardial infarction, both clinically and by means of limb lead electrocardiograms, multiple chest lead cardiograms afford a good means of differential diagnosis. In posterior myocardial infarction, as is well known, there may not be any cardiographic change, or the RS-T segment may be depressed, or the T waves may be very tall. In pulmonary embolism sufficient to cause right ventricular stress there is sharp inversion of the T wave, which is maximal and of the longest duration in the right pectoral lead; usually present, but for a shorter duration in the left pectoral lead, and rarely present, and for the shortest duration in lead IV. Similar changes may occur in all conditions causing right ventricular stress.

Incidence.—I. S. Wright, from an experience of more than 300 cases of thrombophlebitis, believes that pulmonary embolism is probably in more than half the cases missed or wrongly diagnosed. N. W. Barker gives a large series of ileo-femoral thrombophlebitis; in these, fatal pulmonary embolism occurred in 5 per cent.

Treatment

Ligation of femoral veins.—J. B. Sears, dealing with his experience in ligation of the femoral vein for prevention of post-operative pulmonary embolism, states that failure to divide deep veins containing blood clots may result in a major catastrophe. The operation is performed under novocain infiltration, and a vertical incision 10 centimetres in length is made in the femoral triangle over the femoral impulse. The artery is exposed and the vein ligatured just distal to the profunda vein or any other large tributary.

Operative prevention of pulmonary embolism.—J. Homans discusses the exploration, division, and ligation of the femoral and iliac veins in the treatment of some of the forms of thrombophlebitis peculiar to the leg. The chief reason for this surgical treatment is the prevention of pulmonary embolism, and it is pointed out that the so-called 'blood' type, especially that in the deep veins of the calf, is the most likely to cause pulmonary embolism. This thrombophlebitis occurring in active life when the patients are young or middle-aged and free from previous disease, depends for its diagnosis on the following points: lameness on walking, especially when going up or down stairs; such swelling and cyanosis as are present are confined to the leg; absence of oedema from the thigh; the positive dorsi-flexion sign, namely discomfort behind the knee on forced dorsi-flexion of the foot; the swelling and cyanosis are always relieved by a few days' rest in bed, thus contrasting with femoro-iliac thrombophlebitis. If ten days' rest in bed and a cautious return to activity are followed by a relapse, the superficial femoral vein should be exposed and divided. A more difficult problem is presented by thrombophlebitis of the deep veins of the calf occurring when the patient is already in bed, for it often passes without recognition until embolism occurs. Of outspoken phlegmasia alba dolens it is said that if it were not a rather common cause of arterial vasospasm, it would be of little surgical interest. It is otherwise with non-obstructing 'bland' thrombosis of the upper femoral and iliac veins, which is probably an extension from thrombophlebitis of the deep veins of the calf; this soft clot is a source of repeated embolism; exploration of the femoral vein and possibly removal of the soft clot by suction is a method of prevention. Exploration and division of the femoral and iliac veins may cure peripheral vasospasm, especially when the vein has previously been inflamed. Division of the superficial femoral, common femoral, or even common iliac vein following an old, canalized thrombophlebitis, causes little disturbance and may, by relief of reflex vasospasm and by the prevention of back flow in the vessel, be of benefit to the venous circulation.

Heparin therapy.—J. T. Priestley, H. E. Essex, and N. W. Barker present a preliminary report on the clinical use for the prevention of thrombosis and pulmonary embolism of the new non-toxic and crystalline preparation of heparin made from beef lung (A. F. Charles

and D. A. Scott, 1934), which is much more powerful than the original preparation of W. H. Howell and E. Holt (1918). At present the most effective method of its administration is by continuous intravenous injection; the effect of heparin disappears rapidly after its administration is stopped, and after several hours the coagulation time of the blood returns to its previous level. The intravenous administration must be carefully watched and regulated at frequent intervals by estimation of the coagulation time and, if this is done, there is not any serious bleeding. Transient haematuria occurred in several patients. The administration has with a few exceptions been confined to two main groups: (a) those patients with definite evidence of a non-fatal pulmonary embolism, and (b) a few with post-operative thrombophlebitis. An existing thrombus is not affected, but its further growth is inhibited. The amount of heparin needed to keep the coagulation time at a level of 15 to 20 minutes varies much from patient to patient, and in one may be double the amount needed in another. The results of heparin in patients with pulmonary embolism have been most successful. Only 2 embolic fatalities have occurred in patients who have had heparin. Treatment of thrombophlebitis has been less extensive, but when begun early with heparin the duration of the thrombophlebitis is probably shortened. More than 55 patients have been treated.

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(1941) *ibid.*, **16**, 17.

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LUNG DISEASES: BLAST INJURIES

See also pp. 3, 10, 73, and 90 of this volume.

Clinical picture

Chest complications

Results of air-raids.—D. M. Dean, A. R. Thomas, and R. S. Allison report on the state of the chests of 27 patients under treatment for burns or other injuries from high-explosive bombs at close quarters. In only 2 cases was the question of exposure to blast doubtful. Only 6 patients complained of symptoms related to the chest; 16 showed some abnormal physical signs, and 14 abnormal radiological signs. Evidence of serious or gross pathological changes in the chest was absent in all but 2 cases; one of these had signs of collapse of a lobe of the lung, and the other had the signs of a patchy consolidation of the bronchopneumonic type. The authors draw attention to the relative disproportion in the incidence between the symptoms and physical signs in the cases studied; chest complications may arise after explosion blast without definite warning symptoms, and this should encourage the performance of routine examinations even in those who are apparently unaffected by the blasts. The physical signs to be expected are diminished movement of the diaphragm, fullness of the chest, giving it an emphysematous appearance, and impairment of resonance at one or both bases, with or without crepitations. A 'blown-up' or ballooned appearance of the chest, especially at the lower costal margins, is frequent. This may be related to the posture adopted by the patients in bed, or to the presence of an already existing emphysema. This appearance is often associated with diminished movement of the diaphragm. There are radiological appearances of a diminution of rib-expansion, together with slight loss of translucency, particularly on the left side.

Effect on lungs.—S. T. Falla reports a case of injury from bombing which showed the effect of blast on the lungs. The bomb had exploded in an enclosed space, within about 45 feet of the patient. He was treated for a large lacerated wound on the thigh, but died 12 hours after sustaining his injury. Blood was not seen in the mouth at any time, and no symptoms suggesting a pulmonary lesion had been noted. Necropsy showed that the lungs as a whole were not unduly congested, but there were many small recent haemorrhages visible everywhere on the pleural surfaces. The cut surfaces of the lungs showed innumerable bright red points of haemorrhage. The trachea and bronchi showed a number of submucous points of haemorrhage, and there was some blood on the surface of the mucous membranes. No tear was found in any part of the lungs, and no injury was noted in the brain, kidneys, spleen, or any other viscus. Microscopical examination showed generalized arterial dilatation and intense focal capillary dilatation, with exudation of fluid into many alveoli.

G. Hadfield, Joan M. Ross, R. H. A. Swain, J. M. Drury-White, and A. Jordan, in a preliminary investigation on 10 patients considered to have died suddenly, or within a few hours after short-range exposure to high explosives during aerial bombardment, found that, in all but 1 case, gross traumatic lesions were either completely absent or of trivial degree. In each of these 10 cases some degree of capillary haemorrhage into the lung was found. In 2 cases, in which death was considered to be due to compression asphyxia, the haemorrhage

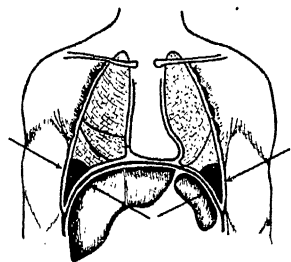
was relatively slight, but the capillary and venous congestion and oedema present were striking, and the air-passages contained only a small amount of blood-stained fluid which was not 'frothy'. In 4 cases in which death was considered to be due entirely to the effects of blast there was free capillary bleeding over large areas in which the respiratory bronchioles, atria, and alveoli showed uniform and considerable over-distension.

G. Hadfield and R. V. Christie report the case of a man, aged 23, who lived for 51 hours after exposure to the detonation of high explosive. In a review of 17 necropsies of such cases, the authors were struck by the variability in the extent of pulmonary haemorrhages, and consider it reasonable to correlate this variation with the period of survival after exposure to blast. In the case reported the areas of haemorrhagic consolidation were surrounded by deep zones of recent bleeding, and the authors are inclined to believe that patients in whom pulmonary haemorrhages develop without external trauma to the thoracic wall after the detonation of high explosive continue to bleed into the lung for a period which may amount to 48 hours or so.

Experimental investigation.—S. Zuckerman reports the results of an experimental investigation, carried out on a large number of mice, rats, guinea-pigs, rabbits, cats, monkeys, and pigeons, of the direct effects of the blast in high explosions. In the war 1914–18 the possibility that blast could directly produce injuries inside the chest or abdomen without superficial damage was only exceptionally recognized, although in 1918 G. Marinesco carried out some experiments with blast on dogs. In the Spanish war observations were made on the subject. In comparatively slight cases of blast produced experimentally there are spots of haemorrhage on the surface of the lungs; in more severe cases there are patches of blood of various sizes; and in very severe examples the whole surface of the lungs is haemorrhagic. Often the haemorrhages follow the lines of the ribs. In some animals with very severe lesions the lungs are completely hepatized by haemorrhage, and there may be lacerations along the lines of the ribs. The lesions are more extensive in animals which survive for some time than in those killed at once. The most vulnerable part of the lungs is the anterior border where lacerations may occur. Microscopically the damaged areas appear as zones in which the alveoli and bronchioles are filled with blood; the alveolar walls are often ruptured, blood coming from the torn capillaries. The factor responsible for the pulmonary lesion is regarded as mainly the impact of the blast wave on the body wall, and not to lowering of the alveolar pressure with rupture of the alveolar capillaries, nor to sudden distension of the lungs with air, alternatives which have been suggested. About 40 per cent of all animals examined, all with pulmonary haemorrhages, showed haemorrhagic lesions in the abdominal organs, the most susceptible being the colon; but the severity of the lesions is not correlated with survival, and the abdominal viscera are much less sensitive than the lungs to blast.

G. Hadfield summarizes the data from 30 necropsies on patients clinically regarded as dying from the effects of blast. In 17 there were bilateral multiple pulmonary haemorrhages, 4 of these with 50 to 75 per cent saturation with carbon monoxide. Hadfield agrees with Zuckerman that there is not any essential difference between the experimental and the human lesions in the lungs. Sections taken through the haemorrhagic areas show that the blood lies almost exclusively in the alveoli and comes from the capillary network which is always considerably dilated and congested. Relatively little blood occupies the airways, but there is always considerable dilatation of the alveolar ducts and bronchioles. The amount of blood in the lungs varies within very wide limits. The areas of haemorrhagic consolidation are quite elastic, but may contain patches suggesting pneumonia. Evidence is brought forward to show that the amount of blood in the lungs increases with the duration of survival, bleeding into the lung continuing for some days; these patients should therefore be immobilized as if they had had a recent large haemoptysis.

Phrenico-costal sinus pneumonia.—Under this title G. R. Osborn describes a condition, apparently not previously recognized but probably not infrequent. Strictly speaking it is not pneumonia, but a contusion due to a peculiar injury of the lateral portion of that part of the base of the lung which enters the phrenico-costal sinus of the pleura on deep inspiration. Many muscular efforts are made with the breath held in full inspiration—that is with this part of the lung fixed in the phrenico-costal sinus. The portion of the lung thus fixed may be 'caught in a pincers movement' consisting, on the right side, of the elbow and liver, and, on the left side, of the spleen and the elbow.



Records of 5 cases with necropsies are given. The first 2 patients, men aged 49 and 55, sustained a relatively trivial but peculiar injury. Had it not been for unexpected complications, acute pulmonary oedema and pulmonary embolism, these 2 men might well have recovered from the strain in the side. Patients 3 and 4, men aged 62 and 63, were delirious, with superficial bruises, and at necropsy the lungs contained the sharply defined wedge-shaped consolidation characteristic of the condition; in one of the men the lung lesion was bilateral. The other special features of the lung lesion are its position, the lateral part of the extreme base, exceptional hardness and weight, sharply defined edges which project from the surrounding lung tissue, and dry and dark cut surfaces. The signs

of contusion, such as injuries to the elbow and the chest, of the diaphragm, liver, or spleen, and a blood-stained effusion with or without flakes of fibrin over the lung lesion, should be looked for. The fifth case, which concerned a girl, aged 17, killed at once in an air raid, threw light on the mechanism of blast injuries to the lung.

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— Ross, Joan M., Swain, R. H. A., Drury-White, J. M., and Jordan, A. (1940) *Lancet*, 2, 478.

Osborn, G. R. (1940) *Brit. med. J.*, 2, 317.

Zuckerman, S. (1941) *Proc. R. Soc. Med.*, 34, 171.

LUPUS ERYTHEMATOSUS

See also B.E.M.P., Vol. VIII, p. 244; Cumulative Supplement, Key No. 1004; and Surveys and Abstracts 1940, p. 395.

Clinical Types

Renal involvement

J. M. Stickney and N. M. Keith analysed the renal conditions, both clinically and at necropsy, in 15 patients with disseminated lupus erythematosus. In only 4 of the cases did the disease end in uraemia with a blood urea of more than 60 milligrams per 100 cubic centimetres. These and 5 others showed fairly constant albuminuria, microscopical haematuria, and casts. In most cases there was a considerable fluctuation in the urinary changes which corresponded quite closely with the severity of the cutaneous symptoms. The renal functions were satisfactory until the final stages of the disease. In 2 cases albuminuria preceded the cutaneous lesions. In 1 case there were cotton-wool exudates, and in 1 there were small haemorrhages in the ocular fundi. In all cases the weight of the kidneys was normal or greater than normal. The most definite lesion was a proliferation of the endothelial cells of the glomerular capillaries. Hyaline thickening of these capillary walls and an irregularity of the basement membrane were also often present. The renal condition is either not an ordinary glomerulo-nephritis or is one of low virulence with slow progress.

Treatment

Sulphonamide compounds

H. W. Barber describes the effects of sulphonamide compounds on lupus erythematosus, and considers that, in those long-standing cases of the disease which appear to be due to streptococcal infection, the sulphonamides offer a valuable method of treating latent and inaccessible foci of infection. In those cases thought to be due to chronic tuberculosis, the drugs have not any therapeutic effect.

U. J. Wile and H. H. Holman treated seven cases of acute disseminated lupus erythematosus with sulphonamide compounds. Definite clinical improvement was noted in 3 cases during the administration of sulphanilamide. In the cases in which sulphanilamide failed, sulphapyridine and promin (the sodium compound of bis(*p*-aminophenyl)-sulphone dextrose sulphonate) did not succeed. Although the results in general were discouraging, the occurrence of some improvement in a few cases warrants the further use of sulphanilamide in cases of this type.

H. H. Hopkins reports a case of acute disseminated lupus erythematosus which appeared to have been precipitated by X-ray therapy after a radical mastectomy for carcinoma. Sulphanilamide was given in a dosage of 3.6 grammes daily for 12 days. The response to this treatment was dramatic. Within 24 hours the temperature fell to 97° F., and complete exfoliation of the affected skin occurred.

F. Glyn-Hughes and A. M. Spence obtained a definite response to sulphonamide therapy in 12 cases of lupus erythematosus. This strongly supports the view that the disease is streptococcal in origin. In 6 cases the disease was cured and there were no relapses. In the other cases, after an initial improvement, the disease remained stationary, or revived. The existence of some latent and resistant focus of infection was probably the cause of failure in these cases. The successful cases included all those patients who had not suffered from the disease for more than a year. In the earlier cases the dosage of sulphapyridine was 1.5 grammes daily, but this was later reduced to 1 gramme and even 0.5 gramme daily. Treatment was continued for about 4 weeks. The authors consider the drug to be almost specific.

Barber, H. W. (1941) *Brit. J. Derm.*, 53, 1.

Barker, N. W. (1940) *Diagnosis and Treatment of Cardiovascular Disease*, Chapter 56, Phila.

Glyn-Hughes, F., and Spence, A. M. (1940) *Brit. med. J.*, 2, 741.

Hopkins, H. H. (1941) *Arch. Derm. Syph., N.Y.*, 43, 833.

Stickney, J. M., and Keith, N. M. (1940) *Arch. intern. Med.*, 66, 643.

Wile, U. J., and Holman, H. H. (1940) *Arch. Derm. Syph., N.Y.*, 42, 1059.

LUPUS VULGARIS

See also B.E.M.P., Vol. VIII, p. 254; Cumulative Supplement, Key No. 1005; and Surveys and Abstracts 1939, p. 420.

Treatment*Grasset's tubercle endotoxoid*

A. R. Davison reports a case of lupus vulgaris which responded to treatment by Grasset's tubercle endotoxoid. This patient was admitted to the Pretoria Leper Hospital as a leper, but the diagnosis was changed to lupus vulgaris.

Davison, A. R. (1941) *Leprosy Rev.*, 12, 18.

LYMPHATIC GLANDS DISEASES

See also B.E.M.P., Vol. VIII, p. 264; Cumulative Supplement, Key Nos. 1006–1009; and Surveys and Abstracts 1939, p. 420; 1940, p. 396.

General Considerations*Lymphatic glands in fat*

Inflamed areas.—E. S. J. King and P. MacCallum state that lymphatic glands draining an inflamed area, or one in which there is a malignant new growth, are more apparent and more numerous than in normal circumstances. All gradations may be found between fat lobules and lymphatic glands. In both experimental and clinical conditions lymphatic glands may be found in situations where they are normally absent. Available evidence indicates that lymphatic glands often arise in fatty tissue.

Tumours

Treatment of lymphosarcoma.—E. R. Pund and F. H. Stelling report 3 cases of lymphosarcoma verified histologically in which clinical cures seemed complete 6, 8, and 11 years after recognition. The usual expectancy of life is stated to average 2 years and 85 to 95 per cent of the patients die before the expiration of 5 years. In one case with lymphosarcoma of the stomach, spontaneous regression occurred after an operation limited to posterior gastroenterostomy. In the 2 other cases surgical removal of early lymphosarcoma of a lymphatic gland resulted in a cure. The histological appearances of the enlarged lymphatic glands showed lymphoblasts invading and displacing the lymphocytes, the capsule and surrounding fat, and destroying the normal architecture of the gland.

King, E. S. J., and MacCallum, P. (1940) *Aust. N.Z. J. Surg.*, 10, 126.

Pund, E. R. and Stelling, F. H. (1941) *Amer. J. Surg.*, 52, 50.

LYMPHOPATHIA VENEREUM

See also B.E.M.P., Vol. VIII, p. 287; Surveys and Abstracts 1939, pp. 155 and 421; 1940, pp. 92 and 398; and p. 109 of this volume.

Clinical Picture*Infection of alimentary tract*

By swallowing of virus.—W. E. Coutts, L. Opazo, and M. Montenegro consider that the constant swallowing of the virus of lymphopathia may infect the alimentary tract, and that spread of infection may possibly be along the lymphatics of the submucosa. Before radical operations are performed radiological investigation of the ileum and colon should be made, and sulphonamide therapy should be tried.

Treatment*Sulphonamides*

F. Hawking reports on the treatment of 4 cases of lymphopathia venereum with sulphanilamide or sulphone, but did not find that recovery occurred sooner than in untreated cases. On the other hand the treatment of patients with chancreoid appeared to be more successful. In the cases of lymphopathia venereum treated with sulphonamides the period spent in hospital was much the same as in cases treated by the usual palliative methods, namely 6 to 29 days, with an average of 18 days.

G. M. Findlay investigated experimentally the relative efficacy of various sulphonamide compounds on mice infected intracerebrally with the virus of lymphopathia venereum. Treatment of the mice daily by mouth with 10 milligrams of drug per 20 grammes of mouse showed that the most active compound was sulphamethylthiazole, followed in order by sulphapyridine, sulphathiazole, sulphanilamide, lutazol (dipotassium *p*-sulphamido-phenylazosalicylate), and disodium 4 : 4'-bis-*o*-carboxybenzoyl : aminodiphenylsulphone.

Chronic unilateral conjunctivitis.—W. Curth, H. O. Curth, and M. Sanders report a case of chronic unilateral conjunctivitis of seven years' duration due to the virus of lymphopathia venereum. Treatment with Frei antigen, given intravenously, was not satisfactory, but the use of sulphanilamide in doses of 80 and 60 grains daily, for several months, was effective in stopping the active process, and in reducing the accompanying oedema and stasis. But vision of the eye had been destroyed several years before.

Inguinal adenitis.—I. L. Schamberg made serochemical and clinical observations on 20 negroes with inguinal adenitis due to lymphopathia venereum, treated with sulphanilamide. Of these, 14 (70 per cent) experienced rapid relief of symptoms, although objective improvement was slower. After 102 to 325 days from the beginning of treatment, 9 of the 16 patients re-examined (56 per cent) were free from any evidence of the disease, and 7 (44 per cent) still showed asymptomatic residua. All the patients showed an initial hyperglobulinaemia which returned toward the normal level as clinical improvement occurred. The author suggests that the increase in blood globulin uniformly seen represents a humoral antibody response

against the virus of the disease, and that its reduction to normal in patients treated early with sulphanilamide shows inhibition of antibody formation through destruction of the virus.

Coutts, W. E., Opazo L., and Montenegro, M. (1940) *Amer. J. Digest. Dis.*, 7, 287.

Curth, W., Curth, H. O., and Sanders, M. (1940) *J. Amer. med. Ass.*, 115, 445.

Findlay, G. M. (1940) *Lancet*, 2, 682.

Hawking, F. (1940) *J. trop. Med. (Hyg.)*, 43, 271.

Schamberg, I. L. (1941) *Amer. J. med. Sci.*, 201, 67.

MALARIA

See also B.E.M.P., Vol. VIII, p. 304; Cumulative Supplement, Key Nos. 1018 and 1019; Surveys and Abstracts 1939, pp. 142 and 423; 1940, pp. 75 and 399; and p. 96 of this volume.

Aetiology

Epidemiology

Transmission by hypodermic syringes.—H. Most found that in New York City, which is an endemic area for malignant tertian malaria, the disease occurred almost exclusively among heroin drug addicts who practised the common use of hypodermic syringes. Infection was direct from addict to addict. The parasite was *Plasmodium falciparum*, and after 5 years of asexual transmission it was still capable of infecting anopheline mosquitoes.

Transmission in stored blood.—E. F. Gordon reports the case of a boy, aged 7, who contracted quartan malaria after the administration of stored blood. Examination of the blood of the donor, who did not give any history of malaria, showed the presence of the plasmodium. The incubation period was between 33 and 44 days after the transfusion. This appears to be the first case of this kind reported. To avoid this the author suggests that a thick drop preparation of the blood should be examined, and that blood should be stored for at least 8 days before use.

Diagnosis

Rapid staining technique

J. W. Field describes a simple and rapid method of staining malarial parasites in thick blood smears. The stain consists of brilliant cresyl blue 1 gramme, disodium hydrogen phosphate (anhydrous) 1 gramme, potassium dihydrogen phosphate 1.25 gramme, and distilled water to 100 cubic centimetres. The blood smears should not be more than 50 μ thick. The smears are rapidly dried by waving in air or a hot-air current, and lightly heat-fixed by passing through a flame for about a second. To stain the smears, the slides are dipped for 1 second into a jar containing the stain, immediately removed, and rinsed for 5 seconds by waving gently in a vessel of clean tap water. When dry they are ready for microscopical examination.

Malaria Therapy

Control of undesirable symptoms

Thio-bismol.—H. N. Cole, G. A. DeOreo, J. R. Driver, H. H. Johnson, and W. F. Schwartz, anxious to find an agent which would temporarily stop the alarming symptoms, namely prolonged remittent fever, physical exhaustion, vascular collapse, persistent vomiting, increasing anaemia, rapidly rising icteric index, and blood urea nitrogen, sometimes occurring during the course of therapeutic malaria employed in the treatment of neurosyphilis, found that although antimony compounds may in part satisfy this demand, certain bismuth salts, especially thio-bismol, are the most satisfactory. Thio-bismol (sodium bismuth thioglycollate) was used in 103 observations; in 92 a single, and in 11 more than one, injection being given. The dosage was 0.2 gramme given intramuscularly. A single injection given just before a chill was nearly always followed within 6 to 12 hours by an afebrile interval. In the prolonged remittent type of fever, a 48-hour respite was the rule. In patients with daily chills (double tertian) one injection also gave a 48-hour rest period. In patients with chills every 48 hours (alternate cycle, tertian), usually only one chill was eliminated, giving an additional 48 hours' rest. In rare cases a single injection entirely terminated the clinical malaria. Repeated injections of thio-bismol stopped therapeutic malaria for as long as 39 days. The authors do not offer thio-bismol as a substitute for quinine in terminating malaria, but as a useful drug in the management of therapeutic malaria, the use of which, by giving a temporary rest, may enable the malaria treatment to be continued. When it is desirable to terminate a course of therapeutic malaria without shock to the patient, an intramuscular injection of thio-bismol and the oral administration of quinine or atabrin (mepacrine hydrochloride) will effect this. With the use of thio-bismol in 263 cases of therapeutic malaria, the death-rate was 2.2 per cent. With the help of the drug it was possible to carry on the course of malaria until the patients had had an adequate number of hours of hyperpyrexia.

Effect of sulphathiazole on rigors

R. Pakenham-Walsh and A. T. Rennie report on the effect of sulphathiazole on the rigors and parasites in a general paralytic inoculated with benign tertian malaria. The maximal daily dosage was 2 grammes, 3 times daily, at intervals of 4 hours. There was a marked decrease in the number of rigors, and the parasite count fell from 90 to 4 per hundred fields, and remained at a fairly low level for 9 days before quinine was given.

- Cole, H. N., DeOreo, G. A., Driver, J. R., Johnson, H. H., and Schwartz, W. F. (1940) *J. Amer. med. Ass.*, **115**, 422.
 Field, J. W. (1940) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 195.
 Gordon, E. F. (1941) *J. Amer. med. Ass.*, **116**, 1200.
 Most, H. (1940) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 139.
 Pakenham-Walsh, R., and Rennie, A. T. (1940) *Lancet*, **2**, 485.

MEASLES

See also B.E.M.P., Vol. VIII, p. 412; Cumulative Supplement, Key No. 1027; Surveys and Abstracts 1939, pp. 77 and 424; 1940, p. 401; and p. 68 of this volume.

Clinical Picture

Complications

Encephalitis and paraplegia.—C. P. Ward reports a case of measles with severe encephalitis. For several days the prognosis for life appeared to be hopeless, but the encephalitis subsided, only to be followed by a transverse myelitis with flaccid paraplegia and a 'cord bladder'. After 9 days of complete paralysis, recovery began, and was complete, except for spastic paresis of the legs noted 2 months later.

Treatment

Prophylaxis

Placental extract and convalescent serum.—H. N. Bundesen, W. I. Fishbein, I. R. Abrams, and R. D. Miller report on 678 susceptible measles contacts inoculated with immune placental globulin. They found that 353, or 52.1 per cent, escaped measles, and that 325, or 47.9 per cent, contracted the disease. Of the 325 in whom measles developed, 293, or 90.1 per cent, went through a modified form of the disease. Of 299 susceptible measles contacts inoculated with convalescent measles serum, 219, or 73.24 per cent, did not contract measles, whereas 80, 26.76 per cent, contracted the disease. Of these 80 children, 74, or 92.5 per cent, had a modified type of the disease. The authors conclude that though convalescent serum seems superior to placental extract, the latter is of value in prophylaxis in large communities because it is more readily available.

Purpura; treatment with vitamin P.—A. A. Miller reports a case of purpura in a boy, aged 5, during the course of measles. On the eighth day of the infection thrombocytopenic purpura appeared. A prominent feature of the illness was haematuria. The gums oozed blood, and there were petechial spots on the buccal mucous membrane, on the hard and soft palate, and on the body and limbs. Hesperidin (vitamin P) was given by mouth, in doses of 0.25 gramme, at 2-hourly intervals; slight improvement was observed after a total of 3 grammes of the vitamin had been administered. Further 3 grammes of hesperidin for 24 hours was followed by great improvement in the haemorrhagic symptoms. The dosage was then altered to 0.25 gramme of the vitamin every 4 hours. The patient rapidly recovered.

Bundesen, H. N., Fishbein, W. I., Abrams, I. R., and Miller, R. D. (1940)

J. Amer. med. Ass., **115**, 104.

Miller, A. A. (1941) *Brit. J. Child. Dis.*, **38**, 1.

Ward, C. P. (1941) *Arch. Pediat.*, **48**, 83.

MEDIASTINUM DISEASES

See also B.E.M.P., Vol. VIII, p. 438; and Surveys and Abstracts 1939, p. 425.

Classification

Traumatic lesions

Mediastinal flutter.—In the course of a comprehensive review of wounds of the chest and abdomen, S. W. Harrington points out that one of the differences in the results of injuries of the two serous cavities is the normal negative pressure in the chest. In an open pneumothorax, due to a penetrating wound, the movements of this lung becomes paradoxical, expanding with expiration and collapsing with inspiration; these competitive respiratory movements of the lungs cause a to and fro passage of air from the bronchi of one lung to the bronchi of the other, and cause a greatly diminished oxygen-content of the alveolar air and consequently of the blood. At the same time an open pneumothorax exerts a serious effect on the heart by the 'flapping' of the mediastinum, which is drawn over to the sound side on inspiration and forced back again on expiration. Of the greatest importance in this mediastinal flutter is its interference with the continuous flow in the great veins leading to the heart. Systolic output depends on diastolic inflow, and mediastinal flutter causes periodical obstruction of both the superior and inferior venae cavae. But not all patients with a penetrating wound present mediastinal flutter, because if the mediastinum or the lung is fixed by adhesions due to previous disease, or if the patient has a high vital capacity, a large opening may be tolerated for some time.

Infections

Tuberculosis.—C. S. Keefer considers that tuberculosis of the mediastinum should include tuberculosis of the lymphatic glands, cold abscess of the mediastinum secondary to disease of the spine, sternum, or lymphatic glands, and chronic fibrous mediastinitis. The diagnosis depends on the symptoms and signs of an infection of the mediastinum, the X-ray examination of the chest, and the anatomical process associated with mediastinal disease.

Tumours

Mediastinal ganglioneuroma.—A. G. James and G. M. Curtis review 33 cases of mediastinal ganglioneuroma, a rare growth consisting of nerve cells embedded in a large amount of fibrillar stroma and arising from the sympathetic nervous system. The growth has a low tendency towards malignancy and this varies inversely with the age of the patient. The only treatment is surgical removal, and X-ray therapy does not appear to be beneficial. In cases in which operation is possible the prognosis is good.

Harrington, S. W. (1940) *Proc. Mayo Clin.*, **15**, 808.

James, A. G., and Curtis, G. M. (1941) *Ann. Surg.*, **113**, 767.

Keefer, C. S. (1941) *Amer. J. Roentgenol.*, **45**, 489.

MEDICO-LEGAL EXAMINATIONS AND REPORTS

See also B.E.M.P., Vol. VIII, p. 453; Cumulative Supplement, Key No. 1030; and Surveys and Abstracts 1939, p. 426; 1940, p. 401.

Mode of Examination*Estimation of age from teeth and jaws*

Significance of appearances.—E. Sprawson, in a presidential address, brought together the information that can be deduced about the individual's antecedents and his life from examination of the teeth and jaws. The age of the individual may be assessed with relative but not absolute accuracy, chiefly from the teeth and to a less extent from the jaws. The rate of wear of the teeth varies with the physical characters of the food and the functional activity of the teeth, the latter varying with the presence of dental caries, pain, the degree of occlusal perfection, and the health and vigour of the individual; deciduous teeth show the wear much more than do the permanent teeth. As regards the jaws, the degree of growth, closure of sutures, measurement of the angle of the mandible, the condyle, and the presence of sockets of teeth or their crypts are significant. Much may sometimes be learned about the diseases of childhood from both the deciduous and the permanent teeth; from the deciduous teeth, the green teeth of icterus gravis neonatorum, which must be distinguished from the green stain common on neglected teeth, and the pink teeth of congenital haematoporphyrinuria, which must not be confused with haemorrhage, are good but rare examples in the deciduous teeth. Transverse linear hypoplasia of the permanent teeth, mainly on the incisors, is evidence of an acute short illness at the time the parts affected were forming. The more common trophic form of hypoplasia, so often seen 20 and more years ago, was due to dietary deficiency. The dental stigmata of congenital syphilis are pathognomonic. 'Mottled' teeth are usually due to excess of fluorine in drinking water. Habits and occupations may leave their marks on the permanent teeth, e.g. the special form of attrition on the maxillary incisors of boot-last makers, the abrasion shown by the smokers of clay pipes, and the rampant caries of the baker or confectioner. Sprawson had seen a professional chocolate-taster who had cervical caries on every tooth in an otherwise almost complete dentition, and mentioned extensive cervical caries in young employees in chemical factories who were exposed to sulphuric and tartaric acids.

Sprawson, E. (1940) *Proc. R. Soc. Med.*, **34**, 1.

MEGACOLON AND ANAL ACHALASIA

See also B.E.M.P., Vol. VIII, p. 470; Cumulative Supplement, Key No. 1031; and Surveys and Abstracts 1939, p. 426; 1940, p. 402.

Treatment*Operative and non-operative*

Acetyl- β -methylcholine bromide.—J. L. Law, discussing the aetiology of megacolon, states that one of the following two working hypotheses is probable: hyperactivity of the sympathetic nerves to the colon, and diminished tonus of the parasympathetic innervation of the colon with associated insufficient relaxation of the internal sphincter. The author employed acetyl- β -methylcholine hydrochloride or bromide in 15 cases. After the colon has been unloaded by enemas and liquid paraffin by mouth, the drug is begun orally in doses of 0.1 gramme half an hour before breakfast, and increased, if necessary, in 2 or 3 days to 0.2 gramme, and after several days, if indicated, further increased by the addition of 0.1 to 0.2 gramme given in the middle of the afternoon. As the drug becomes effective enemas should be discontinued, although not the liquid paraffin. When stabilized on a dosage which produces one or two stools daily, the patient continues on this dosage, with an occasional enema in the event of constipation or distension.

L. H. Barenberg, D. Greene, and L. Greenspan draw attention to the inhibitory action of the sympathetic nerve supply and the stimulating action of the parasympathetic supply upon the colon, indicating excessive sympathetic or diminished parasympathetic activity as a possible cause of congenital megacolon. Sympathectomy has not always been successful and the use of the parasympathetic activator, acetyl- β -methylcholine, is suggested and illustrated by a case report. The patient was observed from the age of 3 months to that of 4 years. Symptoms were: abdominal distension, acute constipation, dry skin, thick tongue, vomiting, high blood-cholesterol, and distended colon. Distension increased, the patient became mentally retarded and showed facial signs of hypothyroidism. At the age of 3 months treat-

ment consisted of thyroid extract; at 6½ months atropine, pituitary extract, thyroid, syntropan (3-diethyl-amino-2:2-dimethylpropanol ester of tropic acid), prostigmin bromide and enemas; for a period of years pituitary extract and mineral oil had temporary effects. Syntropan and depropanex (a deproteinated pancreatic extract) were given for another 2 months without any effect. At 3½ years, 4 centimetres of the right presacral nerve was dissected and the left 4th lumbar ganglion and 1-2 centimetres of the sympathetic chain removed. After 25 days there was not any improvement. Another 3 months of thyroid and pitressin had no effect. Then acetyl-β-methylcholine chloride (mecholy) was given hypodermically in 5 doses of 1 milligram after several days of constipation. Peristalsis began in 3-5 minutes, lasting 20 minutes, with activity of the small intestine. Delayed effects were shown. A combination of 1 milligram of mecholy and 0.25 milligram of prostigmin methylsulphate caused powerful peristalsis, vomiting, passage of faeces, lasting 15 minutes, and slight shock. Medication was discontinued and distension persisted. Law's procedure was used, namely, 2 fl. ounces of mineral oil daily for 5 days, mecholy bromide by the mouth in small doses increasing to 200 milligrams twice a day and then reduced to a stable dose of 200 milligrams a day. Distension and constipation were relieved and physical development returned to normal. The author comments on the failure of sympathectomy which may have been due to incomplete procedure, and suggests that the drug action may have been supplementary to sympathectomy. It cannot be concluded definitely that the response to the drug is permanent.

Barenberg, L. H., Greene, D., and Greenspan, L. (1941) *J. Pediat.*, **18**, 579.

Law, J. L. (1940) *Amer. J. Dis. Child.*, **60**, 262.

— (1940) *J. Amer. med. Ass.*, **114**, 2537.

MENINGITIS

See also B.E.M.P., Vol. VIII, p. 495; Cumulative Supplement, Key Nos. 1033-1040; and Surveys and Abstracts 1939, pp. 125 and 426; 1940, p. 402.

Pneumococcal Meningitis

Course and treatment

Sulphonamides and antiserum.—J. M. Ruegsegger and M. Hamburger report a case of Type III pneumococcal meningitis in which the patient recovered promptly after the administration of sulphathiazole and anti-pneumococcus serum. The initial dose of the drug was 4 grammes, with subsequent doses of 2 grammes every 4 hours. Twelve hours later the patient was given 240,000 units of Type III anti-pneumococcus serum intravenously. The drug was continued for 6 days, until a total of 67 grammes had been given.

A. J. Moss and E. L. Strem report a case of pneumococcal meningitis in a 10-months-old infant, treated by serum and sulphapyridine, with complete recovery. The dosage of sulphapyridine during the first 24 hours was 3 grains per pound of body weight; the drug was continued in somewhat smaller doses during the afebrile period. Apart from cyanosis, no toxic symptoms were noted. The pneumococci present belonged to Type XIV. An intravenous transfusion of 100 cubic centimetres of whole citrated blood was given. This was followed by the injection of 60,000 units of type-specific rabbit antiserum. Within 6 hours of the commencement of serum and sulphapyridine the temperature dropped to 96° F. and did not rise above normal for the remainder of the illness. Next day a further 40,000 units of serum were given intravenously and 20,000 units intrathecally. The patient made a rapid and complete recovery.

F. H. Coleman, analysing the published cases of pneumococcal meningitis treated with sulphapyridine, comes to the following conclusions. The drug has reduced the mortality of the disease from almost 100 per cent to about 35 per cent. To be effective, it must be given in large doses at the onset; at least 6 grammes per day should be given to an adult for the first 4 or 5 days, after which the dosage may gradually be decreased. There is no reliable clinical evidence that anti-pneumococcal serum is of any value in a straightforward case. Frequent lumbar puncture should be avoided, except when it is indicated for the relief of a patient. Sulphapyridine should be continued in decreasing doses for at least a week after the temperature has returned to normal. A patient who is going to recover will almost always show some clinical signs of improvement within the first 3 or 4 days; and if improvement is noticed at all, the patient almost always makes a complete recovery in the end. Provided that dosage has been adequate, cases proving resistant to treatment are due either to a strain of pneumococci insensitive to the drug, or to one which has become tolerant to it.

J. B. Neal, E. Appelbaum, and H. W. Jackson treated 30 cases of pneumococcal meningitis, with 10 recoveries, and 29 cases of meningitis due to *H. influenzae*, with 14 recoveries, by means of sulphapyridine, its sodium salt, or both. A specific serum was also employed. The dose of sulphapyridine was 4 to 8 grammes daily, by mouth. The dose for children over 3 years of age was 4 to 6 grammes, and for infants 2 to 4 grammes. The dose of sodium sulphapyridine was 10 to 15 cubic centimetres of a 2 per cent solution, intrathecally after each spinal drainage.

Pyogenic Meningitis

Treatment

Sulphapyridine in meningitis due to Streptococcus viridans.—W. J. Mitchell, A. G. Bower, and P. M. Hamilton report 6 cases of meningitis caused by *Streptococcus viridans*:

3 patients were treated with sulphanilamide and died; 2 received sulphapyridine and recovered, and the other received sulphapyridine with other remedies and also recovered. Of the 3 patients who received sulphapyridine one was a negro aged 54. His cerebrospinal fluid contained 8,500 cells but direct examination did not show any organisms. He was given sulphanilamide, but after he had received 90 grains the culture of the cerebrospinal fluid showed *Streptococcus viridans*, and sulphapyridine was given, 2 grains every 4 hours for 8 days. On the third day after starting the drug the cerebrospinal fluid cell count fell to 450 and cultures were negative. The second patient was a male aged 22 months. The cerebrospinal fluid contained 1,900 cells and Gram-positive diplococci, and culture showed *Streptococcus viridans*. Sulphapyridine, 1 gramme every 4 hours, was administered. Culture of the cerebrospinal fluid was negative on the following day though Gram-positive cocci were still present; these, however, disappeared on the next day. The patient was discharged on the twentieth day. The third case, in a boy aged 8 years, was first diagnosed as acute poliomyelitis, but subsequently the cerebrospinal fluid showed 12,600 cells and *Streptococcus viridans* on culture. Diagnosis of meningitis was made and treatment with sulphanilamide was started. After 24 hours, sulphapyridine was substituted; as no improvement was apparent after 5 days, sulphanilamide was again given and continued for 3 days. Sulphapyridine was then again given and 2 days later cultures of the cerebrospinal fluid became negative though the general condition did not improve. Uleron (dimethyl disulphanilamide) treatment was then started, and deep X-ray therapy applied to the base of the skull. Within 24 hours clinical improvement was well marked, and on the fifth day the temperature was normal. Subsequently recovery was uneventful.

Haemophilus influenzae infection and sulphapyridine.—Harriet J. Mitchell reports a case of influenzal meningitis in a child 18 months old who recovered after treatment by sodium sulphapyridine, and contrasts this success with the fatal issue in 8 other children under 14 years of age seen in the Mayo Clinic from 1920 to 1940. On admission the blood leucocyte count was 19,200 and the cerebrospinal fluid contained 2,000 polymorphonuclear leucocytes and 70 lymphocytes per cubic millimetre, the sugar being less than 20 milligrams per 100 cubic centimetres. *Haemophilus influenzae* was found in the cerebrospinal fluid. The initial dose was 15 cubic centimetres of a 5 per cent solution of sodium sulphapyridine, and was followed until the third day, when 8 cubic centimetres every 6 hours was tolerated orally. By the eighteenth hospital day the temperature was normal; the cerebrospinal fluid contained only 204 cells and was sterile and the patient greatly improved. On the twenty-first day, however, the temperature rose to 101° F. and the cerebrospinal fluid was cloudy, and it was thought that the vomiting which then occurred might have been due to sulphapyridine; the drug was therefore omitted for 2 days and the temperature rose to 104° F. A relapse occurred, but on the forty-first day the cerebrospinal fluid became sterile, and the child left the hospital after 2 months' residence. The disease is essentially one of childhood, and the mortality, 85 per cent (Fothergill) to 97 per cent (Aleman), is highest under the age of 2 years.

Aleman, Ruth (1940) *Med. surg. J.*, **93**, 25.

Coleman, F. H. (1940) *Lancet*, **2**, 615.

Fothergill, L. D. (1937) *New Engl. J. Med.*, **216**, 587.

Mitchell, Harriet J. (1941) *Proc. Mayo Clin.*, **16**, 298.

Mitchell, W. J., Bower, A. G., and Hamilton, P. M. (1940) *Amer. J. med. Sci.*, **200**, 75.

Moss, A. J., and Strem, E. L. (1941) *Arch. Pediat.*, **58**, 203.

Neal, J. B., Appelbaum, E., and Jackson, H. W. (1940) *J. Amer. med. Ass.*, **115**, 2055.

Rueggsegger, J. M., and Hamburger, M. (1941) *New Engl. J. Med.*, **224**, 686.

METABOLISM

See also B.E.M.P., Vol. VIII, p. 581.

Metabolism of Food Constituents

Investigation of serum proteins

R. F. Loeb reviews the present state of knowledge of serum proteins. Analysis of proteins by the salting-out method, ultra-centrifuge, electrophoresis and the immuno-chemical method, is described. By the last method, qualitative changes in the serum protein fractions of patients may be indicated. Abnormal globulins and proteins have thus been detected in nephrotic patients. The origin of the proteins is discussed. Prothrombin and fibrinogen deficiency in the blood is a recognized test for a deficient liver, whereas damage to other organs does not affect these substances. Prothrombin concentration did not rise after vitamin K administration in the case of degenerative icterus. This fact distinguishes the latter from obstructive icterus. Prothrombin and fibrinogen thus seem to originate in the liver. Although there is a relation between albumin deficiency and liver deficiency, the origin of albumin in the liver is not known for certain. Globulins are thought to originate in the reticulo-endothelial cells of the liver. The depletion of plasma proteins due to undernourishment can be corrected by liberal administration of protein, amino-acids or protein autolysates. Serious albumin depletion may prevent the utilization of the remaining body protein. Beef serum has a high potency in plasma-protein regeneration; beef muscle, liver, egg white have a lower potency and gelatin a low potency. Disturbances in the concentration of albumin and globulin are more important

in diagnosis than their relative proportions. Albumin concentration always diminishes and this upsets the osmotic pressure of the blood, often leading to the accumulation of oedema fluid. Globulin concentration always increases and serious hyperglobulinaemia usually accompanies infections, neoplasms, and metabolic disorders. Too little is known of its significance to be of use in diagnosis. But an increase in globulin without an increase in euglobin concentration is a strong indication of multiple myeloma. Transfusions of plasma proteins may be given in place of whole blood for hyperalbuminaemia when feeding methods of correcting depletion and casein autolysates have failed. They may be given also in the treatment of shock, especially shock due to burns.

Carbohydrate metabolism

Glucose tolerance and staphylococcal infection.—S. H. Jackson, T. F. Nicholson, and W. L. Holman review the clinical and experimental work on the relation between carbohydrate metabolism and infection, and give an account of their work on adult rabbits to bridge the gap between the extremely limited experimental findings and the clinical conditions seen in practice; and to find a more satisfactory explanation for the diversity of the clinical manifestations. A high carbohydrate diet for 6–8 weeks was found to lower the tolerance to glucose in both normal rabbits and in those on a high carbohydrate diet, but the effects of intradermic injection of *Staphylococcus aureus* differed. In normal rabbits there were spreading areas of necrosis of the skin, several of which became confluent, with induration, but little or no production of free pus. These infections varied in their effect on glucose tolerance; 9 out of 14 showed diminution of glucose tolerance, 5 remained within normal limits and 4 gave abnormal curves. Of the other 5 rabbits, 2 were indefinite and 3 showed increased tolerance. In rabbits after 6–8 weeks on a high carbohydrate diet the lesion was generally different, namely, a large swollen lump, filled with pus, with necrosis limited to a small elevation at the summit of the swelling and resembling a boil in man. In 8 out of 9 rabbits the curve of tolerance, high before injection of the staphylococci, was reduced, often to within normal limits; in 4 cases the lesion resembled that in normal rabbits, the tendency was to raise the glucose tolerance. The effect of intradermic injections of staphylococcal toxin was investigated both in normal rabbits and in those after a high carbohydrate diet; the gross appearance of the lesion, necrosis with oedema but little leucocytic infiltration, was the same in both, but the highly dieted rabbits were more affected as regards their general health. The effect of a staphylococcal lesion in rabbits on carbohydrate metabolism is directly related to the degree of localization of the lesion; when the lesion is poorly localized so that a spreading necrotic area results, the infection lowers the power of the body to metabolize glucose, whether in the normal rabbit or the rabbit with a high carbohydrate diet. But if the lesion is well localized the effect of the infection is, if anything, in the reverse direction. The observation that a high carbohydrate diet tends to produce a localized lesion agrees with E. B. Tauber's good results from intravenous injections of glucose in furunculosis.

Jackson, S. H., Nicholson, T. F., Holman, W. L. (1940) *J. Path. Bact.*, **50**, 1.

Loeb, R. F. (1941) *New Engl. J. Med.*, **224**, 980.

Tauber, E. B. (1933) *Arch. Derm. Syph., Chicago*, **27**, 198.

METABOLISM, BASAL

See also B.E.M.P., Vol. VIII, p. 588; and Surveys and Abstracts 1939, p. 432.

Basal Metabolism in Disease

Hypothyroidism and hyperthyroidism

From investigation of the carbohydrate tolerance in hypothyroidism and hyperthyroidism, T. Crawford reports that in hypothyroidism carbohydrate tolerance is impaired. This impairment is due to a general slowing of the processes of katabolism, and possibly also to a diminution in the rate of storage of carbohydrate. The low oral blood-sugar curve which often occurs and accounts for the statements that carbohydrate tolerance is increased in hypothyroidism, is due to slow absorption of the carbohydrate from the bowel. In hyperthyroidism also there is impairment of carbohydrate tolerance, the fault being traceable to defective glycogen formation. This is probably due to the excessive secretion of thyroxine causing an increased liberation of adrenaline, which in its turn mobilizes hepatic glycogen and inhibits its reformation.

T. Crawford (1940) *Arch. Dis. Childh.*, **15**, 184.

MIGRAINE

See also B.E.M.P., Vol. VIII, p. 604; Surveys and Abstracts 1939, p. 433; 1940, p. 408; and p. 91 of this volume.

Aetiology

Relation to hypertension

Headaches.—J. W. Gardner, G. E. Mountain, and E. A. Hines, Jun. discuss the relation between migraine and hypertension, and between migraine and hypertension headaches. The characteristics of the typical hypertension headache are that it is present on awakening, reaches its greatest intensity before breakfast, and disappears during the early morning; it is usually occipital and only seldom unilateral; it varies from a dull ache to severe bursting or throbbing pain; and rarely it may be accompanied by nausea and vomiting and preceded

by a sensory aura. Of 100 (males 38, females 62) hypertensive patients at the Mayo Clinic the ages varied from 20 to 65 years, the great majority being between 40 and 60. As a control series, 100 patients with normal blood pressures were selected at random at the clinic. Of the 100 hypertensives, 79 either were the subjects of migraine or had been so in the past, whereas in the controls the incidence of migraine was 15 per cent only; this figure was confirmed by noting that among the total registrations during 1938 migraine was recorded five times as often in hypertensives as in other patients. Of the 79 hypertensives associated with migraine, 56 were still liable to migrainous symptoms after the onset of hypertension. The incidence of hypertensive headaches was as follows: 44 of the 100 hypertensives; 48 per cent (38 patients) of the 79 hypertensives with migraine; and 28 per cent (6 patients) of the 21 hypertensives without migraine. The association between the two types of headache is shown by the following statistics. Of the 56 hypertensives in whom migraine persisted, 37 per cent (21 patients) had in addition hypertensive headaches; of the 23 hypertensive patients who lost their migraine at the onset of hypertension, 69 per cent (17 patients) developed hypertensive headaches. There is thus a distinct association between the incidence of migraine and hypertension, and the authors suggest that vasoconstriction is an aetiological factor in both conditions; this may also be associated with genetic factors and certain types of personality. These figures also demonstrate the association between two types of headache, and indicate that among hypertensives those who have previously had migraine are more likely than others to experience hypertensive headaches.

Diagnosis and Differential Diagnosis

Migrainous neuralgia

Alcohol treatment.—W. Harris describes 5 cases of migrainous neuralgia, a violent type of migraine distinguished from the ordinary form of migraine by the absence of premonitory symptoms and the rarity of subsequent nausea and vomiting, and from trigeminal neuralgia by the absence of trigger zones and by the longer duration of attacks. The author's treatment is, first, local alcohol piqure and infra-orbital or supra-orbital alcohol injection, which gives relief for several months, and, later, alcohol injection of the Gasserian ganglion, which gives more lasting and probably permanent cure. Of 29 patients treated by the author, 19 patients were completely relieved, and 5 much improved.

Treatment

Oxygen inhalation

W. C. Alvarez and A. Y. Mason report the results of the inhalation by the B.L.B. apparatus of practically undiluted oxygen. This work was carried on for 20 months, and 97 patients with headaches of several kinds were treated. It was found that 80 per cent of migrainous headaches were either stopped or much relieved. Among non-migrainous patients only 24 per cent were helped immediately and another 16 were relieved from pain soon after leaving the laboratory; taking the immediate and late good results together, 28 per cent of persons with non-migrainous headaches were helped decidedly and 12 got some help. In apparently typical migraine 42 per cent of the patients were completely relieved, 44 per cent were helped, 2 per cent obtained delayed relief, and 12 per cent no benefit. There are thus 4 chances in 5 that inhalation of oxygen will give the migrainous patient relief, whereas in non-migrainous headaches there is about 1 chance in 3 that benefit will result from the treatment.

Alvarez, W. C., and Mason, A. Y. (1940) *Proc. Mayo Clin.*, **15**, 616.

Gardner, J. W., Mountain, G. E., and Hines, E. A., Jun. (1940) *Amer. J. med. Sci.*, **200**, 50.

Harris, W. (1940) *Lancet*, **2**, 481.

MOTOR NEURONE DISEASE

See also B.E.M.P., Vol. VIII, p. 611; Surveys and Abstracts 1940, p. 409; and pp. 5 and 50 of this volume.

Treatment

Amyotrophic lateral sclerosis

Vitamin E.—P. G. Denker and L. Scheinman treated 15 patients with amyotrophic lateral sclerosis with α -tocopherol (vitamin E) in large doses both orally and parenterally. Results of any value were not obtained. Two patients with advanced sclerosis continued to go downhill, another 2 became progressively more paralysed during treatment, and 11 did not show any improvement. Four of the patients received an average of 250 milligrams daily, and, in addition, 100 milligrams of vitamin B₆.

Denker, P. G., and Scheinman, L. (1941) *J. Amer. med. Ass.*, **116**, 1893.

MOUTH DISEASES

See also B.E.M.P., Vol. VIII, p. 620; Cumulative Supplement, Key Nos. 1084–1090; and Surveys and Abstracts 1939, p. 434; 1940, p. 410.

Stomatitis

Treatment of gingivitis

Chromium trioxide.—C. H. Smith and H. B. Johnson find that chromium trioxide (5 to 7 per cent) is the only local application of the slightest value in the treatment of acute gingivostomatitis. Improvement begins promptly, and the duration of the disease is shortened,

especially when treatment is begun early. Pain on feeding is much relieved, and the solution is also of value in relieving the pain and in shortening the duration of gangrenous stomatitis, the common 'canker sore'. There is not any danger of a caustic effect or of gum atrophy. The technique of use is important; if old enough to do so, the patient rinses his mouth with a mouth-wash. The kind of mouth-wash is not important. In the presence of much accumulation of sordes or sloughing material on the ulcerated areas, a weak solution of hydrogen peroxide should be used before the mouth-wash. Several swabs of cotton-wool wound tightly on wood applicators are prepared; these should be $1\frac{1}{2}$ inches long and about the diameter of a lead pencil. The gums and ulcers are dried carefully with a swab, then another swab is dipped in the chromic acid solution (5 to 10 per cent in water) and applied directly to the ulcers and the inflamed edges of the gums. Some of the solution is gently worked in between the gums and teeth. This treatment is repeated twice daily for from 1 to 3 days, then once a day. Between treatments the patient can use a mouth-wash. The general treatment is that of any febrile illness.

Ascorbic acid.—H. G. Campbell and R. P. Cook, during a period of 10 weeks, found that out of a total of 505 new patients seen at the Dundee Dental Hospital 18 were suffering from gingivitis, painful and bleeding gums, a condition which was usually spontaneous. In no case could the gingivitis be attributed to trauma, calculus, or the administration of drugs. There were not any other gross signs of a pre-scorbutic state. Fourteen of the 18 patients were treated with massive doses of ascorbic acid; a daily dose of 300 milligrams of ascorbic acid was given until examination of the urine, by Harris and Ray's saturation test, showed that the patient was saturated with the vitamin; usually the total amount of ascorbic acid taken was 2,000 milligrams. During this treatment no dental measures, such as scaling or the use of mouth-washes, were given. Usually bleeding from the gums stopped on pressure after 4 days of treatment. Of the 14 patients 4 failed to co-operate; the others reacted favourably. A maintenance dose is recommended. These results apparently indicate that lack of ascorbic acid is one important factor in the causation of such cases of gingivitis.

Pellagra

'Sore mouth' and vitamin B₃.—According to D. F. Moore, the condition called 'sore mouth' in the League of Nations Report of 1937 is pellagrous and not, as stated, due to vitamin A deficiency. Further, some nervous lesions, as well as some defects of vision, and those affecting locomotion, are of this nature and not due to vitamin A deficiency. A wider use of red palm oil as a food in countries in which the population is known to be deficient in vitamin A is suggested.

Tongue

Black hairy tongue

Caused by Micrococcus albicans.—C. B. Kennedy and J. K. Howles report 2 cases of black hairy tongue which are of interest because of the similarity of their histories and of the cultural findings. Both patients before the onset of the condition had laid their cigarettes on wood covered with a black hairy growth similar to that which later appeared on their tongues. From both tongues *M. albicans* was cultured, and this organism was also found on the specimen of wood produced by one of the patients.

Carcinoma of Cheek

Aetiology

Tobacco chewing.—H. L. Friedell and L. M. Rosenthal support the view that chewing tobacco is an aetiological factor of cancer of the mouth. Analysis of 8 cases in which the disease occurred confirmed the view that carcinoma develops at the point in the mouth where the quid of tobacco is held. The lesions in such cases have a distinctive appearance; they are of a papillary verrucoid character, covered and surrounded by patchy areas of leucoplakia. Moderate induration only is present, and there is an absence of deep infiltration into the sub-mucosal tissues. The lesions grow slowly, and are late in forming metastases. Radium therapy gives good immediate results.

Jaws

Tumours and swellings

Non-malignant ulcer.—H. T. Simmons describes a non-malignant ulcer of the mouth, which he considers is worthy of recognition as a definite clinical entity. The swelling lies in the sulcus between the cheek or lip and the gum, and is situated anteriorly to one or other side of the midline. It is much more common in the lower than in the upper jaw, and in women than in men. A series of ridges are formed which run parallel to the line of the alveolus, and are slightly deeper in colour than the surrounding mucosa. There are always two or more ridges, about an eighth of an inch in thickness, and as much as a quarter of an inch in height, and after running for an inch or more along the gum they gradually slope away into the normal tissues. The ridges are covered with mucous membrane, but ulceration exists in the deeper parts of the furrows. On palpation the tumour is surprisingly hard. Little movement of the deeper tissues can be detected because the swelling is anchored to the alveolus by the innermost furrow. There is little tenderness except during attacks of inflammation which occur at infrequent intervals. The gum is always edentulous, and advanced atrophy of the alveolus makes the denture very loose-fitting. Microscopically the epithelial surface is irregular, but, although it extends fairly deeply into the underlying stroma, it is everywhere limited by a

definite *membrana propria*. The diagnosis from carcinoma is not difficult; the hypertrophied portions are not friable, and bleeding does not occur. The ulceration is confined to the deepest portions of the furrows. There is not any involvement of the regional lymphatics.

Campbell, H. G., and Cook, R. P. (1941) *Brit. med. J.*, **1**, 360.

Friedell, H. L., and Rosenthal, L. M. (1941) *J. Amer. med. Ass.*, **116**, 2130.

Kennedy, C. B., and Howles, J. K. (1940) *Arch. Derm. Syph., N.Y.*, **42**, 566.

Moore, D. F. (1940) *J. trop. Med. (Hyg.)*, **43**, 190.

Simmons, H. T. (1941) *Brit. med. J.*, **1**, 119.

Smith, C. H., and Johnson, H. B. (1940) *J. Pediat.*, **17**, 1.

MUMPS

See also B.E.M.P., Vol. IX, p. 1; Cumulative Supplement, Key No. 1092; and Surveys and Abstracts 1939, p. 435; 1940, p. 412.

Complications

Nervous system and sense organs

Polyradiculitis myelitis and herpes zoster.—I. Snapper reports the occurrence of mumps in a boy, aged 6 years, in whom polyradiculitis and myelitis with herpes zoster occurred. The author lays stress on the importance of involvement of the nervous system in mumps: it may be present in cases without clear-cut neurological signs. The finding of many lymphocytes in the spinal fluid sometimes leads to an erroneous diagnosis. This is particularly true if the meningeal signs appear before the swelling of the parotid glands occurs.

Snapper, I. (1940) *Chin. med. J.*, **58**, 79.

MUSCLE DISEASES

See also B.E.M.P., Vol. IX, p. 11; Cumulative Supplement, Key Nos. 1093–1099; and Surveys and Abstracts 1939, p. 436; 1940, pp. 68 and 412.

Myositis

Dermato-myositis

Compared with systemic lupus erythematosus.—In 1940 H. Keil contributed a paper on dermato-myositis and systemic lupus erythematosus, consisting of a clinical report of five transitional cases, with a consideration of lead as a possible aetiological factor. He now follows this up by a comparative study of the essential clinico-pathological features. Among the clinical phenomena that may occur in both these diseases are fever, pains presumably articular, cutaneous and oral lesions, sensitivity to sunlight, symptoms of Raynaud's disease, enlarged lymphatic glands and spleen, leucopenia, a purpuric tendency, moderate hypertension, renal disease (much commoner in lupus erythematosus), alopecia of the scalp, and sterile blood cultures. Both diseases may run an afebrile course. In spite of these similarities, close attention to clinical details may allow a distinction to be made. Systemic lupus erythematosus shows an overwhelming predilection for young women who often show an unusual sensitivity to sunlight. Dermato-myositis is more likely than lupus erythematosus to occur in males; but both diseases may occur at all ages. The following point to a diagnosis of dermato-myositis: (1) early or initial involvement of the eyelids by a peculiar form of erythematous and telangiectatic oedema; (2) atrophic areas, soft or hard, over the small joints of the fingers, occasionally about the larger joints and sometimes on the trunk; (3) large areas of diffuse erythema in relation to large masses of simultaneously affected muscles and subcutaneous tissues; (4) occasionally a high degree of hypertrichosis on areas previously inflamed; (5) the presence of peculiar white areas on the tongue and oral mucosa; and (6) peri-ungual changes. Endocarditis occurs in 30 to 50 per cent of the cases of systemic lupus erythematosus. In E. Libman's first case in 1911 of atypical verrucose endocarditis (Libman-Sachs disease) there was acute lupus erythematosus. In typical dermato-myositis the endocardium seems to escape, and enlargement of lymphatic glands, although it may occur, is less common than in systemic lupus erythematosus, in which there is involvement of the serous membranes (polyserositis, pleurisy, dry and with effusion). The prognosis is much better in dermato-myositis than in systemic lupus erythematosus. It has been suggested that these two diseases, and especially systemic lupus erythematosus, are involved through the blood supply and so grouped with other conditions under the generic head of 'diffuse vascular disease'. This opinion is critically examined but not accepted by the author.

Metabolic disturbances.—W. J. Griffiths, dealing with the biochemical aspects of dermato-myositis, states that the creatinuria present suggests a disturbance of carbohydrate metabolism in the muscles. Whether this and the peripheral insulin resistance which is also present lead to the degenerative changes in the muscles, or whether the sequence of these events is reversed, cannot at present be determined. The metabolic disturbances in the condition are strikingly similar to those present in diseases known to be endocrine, such as acromegaly and pituitary basophilism.

Complications.—M. S. Hecht reports 5 cases of dermato-myositis, in 3 of which the patients recovered. Four of these cases were complicated by calcinosis universalis. In 2 patients intercurrent attacks of erysipelas occurred, and in another streptococcal cellulitis. In all cases involvement of muscles was wide-spread and severe. Cutaneous manifestations varied. In 3 cases gingivitis occurred. Eosinophilia was present in 3 cases, and severe anaemia in 1.

Muscular Dystrophies*Defect of gluteus medius*

Postural treatment.—H. O. Kendall and F. P. Kendall discuss abnormalities associated with slight weakness and paralysis of the gluteus medius muscles. In a side-lying test a normal gluteus medius will abduct and externally rotate the lower limb under high resistance; a weakened muscle has less power. In the standing test in which one foot is raised, a normal gluteus medius can level the pelvis by pulling on the opposite side; a weakened muscle allows internal rotation of the lower limb and forward tilting of the pelvis. A paralysed muscle cannot perform either test. With a weakened muscle the pelvis rides up on the weak side in the ordinary standing position and causes apparent adduction of the lower limb. The strain may be relieved by lifting the pelvis on the opposite side by a straight raise on the shoe. Whether rotation is used depends on the individual case. Inner border lifts on both shoes are often indicated for this. With severe muscular weakness the pelvis tilts down on the weak side causing apparent abduction and slight extension resulting in excessive strain on the opposite muscle. A firm support transferring the weight from the pelvis to a leg brace is indicated and not a lift on the side opposite the weakness as in the previous case, except when the lower limb on the weak side is actually short. Slight muscular weakness is accompanied by a C-curve of the spine towards the normal side, by pain due to lateral and rotary changes of the pelvis, and by a lowering of the shoulder and by straining the neck muscles. Severe muscular weakness is accompanied by a lumbar curve towards the weak side. Lower limbs of different length can be equalized by a tilting of the pelvis only when hip-joint motion is unrestricted. An apparently long lower limb due to muscular weakness may be actually shorter than the other when supine, and therefore measurements for correction must be made in the standing position. Imbalance is less pronounced in severe muscular weakness because the compensating mechanism is better developed.

Tumours*Intramuscular lipoma*

In the soleus.—H. O. E. Hoffmann and R. K. Ghormley record a case, in a woman aged 42, of a large benign lipoma arising inside the soleus muscle. Swelling of the right calf had existed since early childhood, and before the operation and complete removal of lipoma weighing 2,160 grammes and measuring 22 × 18 × 11 centimetres, the circumference of the right calf was 20 centimetres (8 inches) more than that of the other leg. The patient had not had any pain, but it had been suggested to her that the swelling might be malignant; she also disliked it from a cosmetic point of view and on economic grounds, as she was obliged to have stockings specially made for her. The tumour which was entirely inside the sheath of the soleus, the upper part of which was destroyed, differed from most large lipomas involving the limbs; the latter usually lie between the muscular sheaths or more often in the pericapsular fat around the joints.

Griffiths, W. J. (1940) *Brit. J. Derm.*, **52**, 295.

Hecht, M. S. (1940) *J. Pediat.*, **17**, 791.

Hoffmann, H. O. E., and Ghormley, R. K. (1941) *Proc. Mayo Clin.*, **16**, 13.

Keil, H. (1940) *Arch. intern. Med.*, **66**, 109.

Kendall, H. O., and Kendall, F. P. (1941) *Physiotherapy Review*, **21**, 131.

MYIASIS

See also B.E.M.P., Vol. IX, p. 58; Cumulative Supplement, Key No. 1106; and Surveys and Abstracts 1939, p. 440.

Larva Migrans*Treatment*

H. H. Bayley recommends the following treatment for larva migrans. The skin is dried thoroughly and cleaned with alcohol. The affected area, after being cleared with cedar-wood oil, is examined with the $\frac{3}{8}$ inch objective of a dissecting microscope. After the position of the larva has been noted, the skin is cleaned and 2 minims of procaine solution, 1 in 1,000, is employed to desensitize an area half an inch in diameter with the larva in the centre. A cautery is then applied until a small burn is produced. Sulphanilamide, 7½ grains, is given for 2 days, to prevent bacterial infection of the burrow. No further treatment is necessary.

Bayley, H. H. (1941) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 399.

MYOPIA

See also B.E.M.P., Vol. IX, p. 66; and Surveys and Abstracts 1939, p. 129; 1940, p. 417.

Aetiology*After sulphonamide therapy*

E. A. Rittenhouse mentions that several cases of transitory myopia have been noted after the use of sulphanilamide, and reports a further case of this condition after the administration of sulphapyridine. This patient, a man of 34 years of age, had taken a total of 120 grains of sulphapyridine. He complained of blurred vision, of seeing haloes round lights, and of diplopia. He could see small print only when it was held close to his eyes. On cessation of the drug, the myopia quickly disappeared.

Rittenhouse, E. A. (1940) *Arch. Ophthalm.*, N.Y., **24**, 1139.

NAILS, DISEASES OF

See also B.E.M.P., Vol. IX, p. 83; and Surveys and Abstracts 1939, p. 441; 1940, p. 418.

Dystrophies*Transverse lines*

Aetiology.—Z. T. Wirtschafter and S. Littman believe that the occurrence of transverse furrows of the nails may be due to any process which alters metabolism in the stratum germinativum, which is the only germinating layer of nail growth. The nutrition of this layer is diminished in direct ratio with the diminution of the nutrition of the organism, a fact which would explain the occurrence of transverse furrows in pathological conditions such as prolonged fevers, malaria, tuberculosis, and other debilitating illnesses.

Longitudinal striation

General incidence.—W. H. Kaufman found that 42, or 8.4 per cent, out of 500 people had recognizable longitudinal striation and palpable ridging of the finger-nails. Thirty-eight, or 7.6 per cent, showed similar changes in the toe-nails. This suggests that onychorrhexis is common, and is not therefore of much specific diagnostic value.

New Growths*Glomus tumour*

J. D. N. Nabarro reports a case of glomus tumour in a woman, aged 38, who had suffered from pain in the left ring-finger, radiating up the arm to the shoulder, for 10 to 12 years. Squeezing or accidentally knocking the finger gave rise to an intense burning pain for a few seconds. The pain was provoked by cold and was worse during the winter; it was alleviated by warmth, but heat brought on throbbing. Examination showed, in the centre of the nail of the ring-finger, a small purple patch, 3 millimetres long by 2 millimetres broad. The surface of the nail was quite smooth and did not show distortion. Characteristic variations in pain were elicited by immersion of the hand in hot and cold water. Operation was performed, and microscopical examination of the tumour revealed a typical glomus tumour.

Kaufman, W. H. (1941) *Urol. cutan. Rev.*, **45**, 200.

Nabarro, J. D. N. (1940) *Brit. med. J.*, **2**, 416.

Wirtschafter, Z. T., and Littman, S. (1940) *Arch. Derm. Syph., N.Y.*, **42**, 874.

NARCOLEPSY AND CATAPLEXY

See also B.E.M.P., Vol. IX, p. 91.

Clinical Picture*Mental symptoms*

W. Locke and A. A. Bailey report a case of narcolepsy in a woman, aged 25, in whom, in addition to attacks of narcolepsy and cataplexy, there were mental symptoms suggesting paranoia. Thus she had auditory hallucinations, and visual hallucinations when she was falling asleep. Her behaviour at times warranted committal to a psychiatric hospital. There was, however, a degree of insight and understanding much greater than in cases of schizophrenia. Her personality appeared to be rather well organized, and this was especially true after benzedrine sulphate had been administered for two or three days.

Locke, W., and Bailey, A. A. (1940) *Proc. Mayo Clin.*, **15**, 491.

NECK: TUMOURS AND OTHER MORBID CONDITIONS

See also B.E.M.P., Vol. IX, p. 104; and Surveys and Abstracts 1939, p. 442.

Cysts*Pseudo-laryngocele (cervical aerocele)*

F. R. Kilpatrick records under the above title a condition which differs from those factors recognized as characteristic of a laryngocele. The patient was an emaciated woman, aged 32 years, with extensive tuberculosis of the right lung and a left-sided pneumothorax. Tuberculous ulceration of the anterior laryngeal commissure perforated the thyroid cartilage and thus gave rise to a painless air-containing cavity in the soft tissues of the neck, with its long axis vertical, from the hyoid bone to a point half an inch above the jugular notch, and laterally bounded on each side under the sternomastoid muscles. It was tympanitic on percussion.

Kilpatrick, F. R. (1940-41) *Guy's Hosp. Rep.*, **90**, 15.

NEMATODE INFECTIONS, INTESTINAL

See also B.E.M.P., Vol. IX, p. 125; Cumulative Supplement, Key Nos. 1126-1130; and Surveys and Abstracts 1940, p. 419.

Oxyuriasis*Incidence and Treatment*

In children.—M. J. Miller and L. Choquette record a survey of the incidence of *Oxyuris vermicularis* (threadworm or pinworm) among children in a village in Quebec made with the help of the anal N.I.H. swab devised by M. C. Hall (1937). The number of children examined was 198 (boys 117, girls 81) between the ages of 6 and 16 years. The number of positive cases was 65, or 33 per cent; boys were infected in 29 per cent and girls in 38 per cent; the maximal incidence was at the age of 9-10 years. The authors, with the collaboration of W. Audet,

R. F. Kelso, and J. A. Guenette, contribute the result of the treatment of 29 children, between the ages of 6 to 13 years, by the oral administration of gentian violet tablets, $\frac{1}{2}$ grain for those 10–13 years of age, and $\frac{3}{8}$ grain for those 6–9 years old, 3 times a day for 10 days. Three children only were not cured, so that the treatment was successful in 90 per cent. Untoward effects, mild gastro-intestinal irritation, were negligible in both degree and incidence. The symptoms due to the infestation were anal pruritus in at least half the cases, nervousness, restless sleep, and nocturia.

Pathogeny and symptoms

N.I.H. swab examination.—T. H. Weller and C. W. Sorenson found that among 505 children examined by the 'N.I.H. swab' method, the incidence of enterobiasis (*Oxyuriasis vermicularis* or *Enterobius vermicularis*) was 19 per cent. A higher incidence of 23 per cent was found among girls than among boys (15 per cent). The symptoms consisted of anal pruritus, anal skin lesions, enuresis, loss of appetite, nausea and vomiting, vague intestinal pain, diarrhoea, loss of weight, and night restlessness.

Hall, M. C. (1937) *Amer. J. trop. Med.*, **17**, 445.

Miller, M. J., and Choquette, L. (1940) *Canad. med. Ass. J.*, **43**, 453.

— — Audet, W., Kelso, R. F., and Guenette, J. A. (1940) *Canad. med. Ass. J.*, **43**, 455.

Weller, T. H., and Sorenson, C. W. (1941) *New Engl. J. Med.*, **224**, 143.

NEPHRITIS AND NEPHROSIS

See also B.E.M.P., Vol. IX, p. 134; Cumulative Supplement, Key Nos. 1131–1141; Surveys and Abstracts 1939, p. 443; 1940, p. 420; and p. 2 of this volume.

Morbid Anatomy

Chronic glomerulo-nephritis

Calcium plaques (Randall).—In the course of a naked-eye examination of 1,070 pairs of human kidneys to determine the incidence of the calcium plaques described by A. Randall (1937) on the papillae in the renal sinus, into which the renal tubules discharge, V. Vermooten found that they occurred in 8.3 per cent, and, further, described another condition of the papillae in 40 bodies, which it is proposed to call the 'snow-capped papilla'. It usually occurs in elderly patients with arteriosclerosis, cardiac failure, or both. The white colour is due to a great mass of relatively non-vascular collagen fibres which may compress, dilate, or separate the urinary collecting tubules, and may contain calcium. Usually more than one papilla is affected. It is thought that a further stage of the 'snow-capped' papilla may be Caulk's 'calcareous papillitis' (1912) and the 'calcium infarction' of Randall (1940). The nature and mechanism of this overgrowth of fibrous tissue and its later calcification are now under fuller investigation.

Relation of Nephritis to Hypertension

Treatment

Magnesium sulphate.—M. I. Rubin and M. Rapoport agree that the introduction of magnesium sulphate by K. D. Blackburn and his co-workers to lower hypertension in acute glomerulo-nephritis has proved its efficacy, but bring forward clinical evidence against the view that the fall of blood pressure is due to dehydration. Thus the intravenous administration of hypertonic sucrose produces diuresis, and generalized and cerebral dehydration, without lowering the blood pressure; indeed it occasionally raises the blood pressure. The opinion that cerebral oedema is responsible for vasospasm and hypertension is mentioned but not supported. The authors suggest the magnesium sulphate lowers the blood pressure in acute nephritis by relaxing the existing generalized vasospasm through local action on the smooth muscle of the small blood vessels.

The vicious circle in chronic Bright's disease

In a comprehensive article describing an experimental research on 'The Vicious Circle in Chronic Bright's Disease: Experimental Evidence from the Hypertensive Rat', C. Wilson and F. B. Byrom (1941) follow up their experimental research in 1939. In that research persistent hypertension was produced in 35 rats by partial occlusion of one renal artery; the opposite (unclamped) kidney showed lesions closely resembling those found in human malignant hypertension, namely acute fibrinoid necrosis of the arterioles, endarteritis of the medium-sized arteries, acute changes in the glomeruli, including focal necrosis of the tuft, proliferative glomerulitis, capsular adhesions, and haemorrhagic infarction, and round-celled infiltration in the interstitial tissue. The absence from the clamped kidney of the lesions present in the unclamped kidney was attributed to the protective action of the clamp, in preventing hypertension from reaching the renal arterial system distal to it. In the present expanded research, experimental hypertension was produced in 126 rats of both sexes by the silver clip method of compression of the renal artery in 197 rats. The systolic blood pressure was recorded weekly in all rats, and more often in some rats, under ether anaesthesia by the plethysmographic method of Byrom and Wilson. Blood-urea estimations were made. The rats were killed or died at intervals ranging from 5 days to 46 weeks after the constriction of the renal artery. Histological examinations were made on 116 rats, at first of most of the organs, but later only from the kidneys, pancreas and mesentery, and heart, as these were the sites of election of the vascular changes. Among the numbers of these examinations were

kidney 114, heart 102, pancreas and mesentery 96, and liver 31. The effects of clamping of one renal artery on the blood pressure varied: (1) a steep rise usually to 180–200 millimetres of mercury during the first post-operative week, often with severe constitutional symptoms, followed by death or by survival with persistent hypertension; (2) a gradual rise for several weeks to a high level (180–200 millimetres of mercury); and (3) a gradual and moderate rise to 150–160 millimetres of mercury. Some rats had not developed hypertension at the time they were examined. The unclamped kidney commonly showed compensatory hypertrophy and a granular surface, and histologically chronic changes closely resembling those of chronic hypertensive Bright's disease. The clamped kidney showed as a rule simple atrophy. In 27 rats the clamped kidney was excised, and in 18 of these 27 there was residual hypertension which may give rise to lesions in the remaining kidney. The vicious circle consists in arterial hypertension causing vascular changes which by reducing the blood-flow through the kidney aggravates the hypertension. It is regarded as probable that malignant hypertension has in its later stages a renal component. This research has an obvious bearing on the classification of Bright's disease and explains the unsatisfactory nature of many of the classifications put forward from time to time by both clinicians and pathologists.

Clinical Picture

Glomerulo-nephritis: acute

In children.—S. L. Ludbrook analyses the aetiology, symptoms, complications, treatment, and immediate prognosis in 105 cases of acute nephritis in children up to the age of 15 years. He confirms the close relation between infections due to haemolytic streptococci and acute nephritis. The curves of the annual incidence of acute nephritis and scarlet fever were found to be almost identical. There was a close relation between the rise in vascular tension and cerebral complications. Uraemia, as indicated by a considerable rise in the blood nitrogen, was rare in acute nephritis. The incidence of cerebral complications increased with the age of the patient, no case being noted under the age of 7 years. With regard to treatment, in all cases a normal fluid intake was maintained by mouth, or parenterally if the patient was unconscious; in no case was there any increase in oedema as a result of free administration of fluids. Of 60 patients under observation for an average of over 6 years after the attack, 97 per cent were cured. The author concludes that the ultimate prognosis in the acute nephritis of childhood is very good.

Course and Prognosis

Glomerulo-nephritis

In children.—F. S. Gachet reports observation on the course and prognosis of haemorrhagic nephritis in 188 children. Diagnosis was based on albuminuric levels, blood and casts in the urine, oedema, hypertension, anaemia, and nitrogen retention. Successive clearance tests were made at short intervals during the acute stage to establish some correlation between the progress of clearance and the outcome of the disease. The tests showed that when the disease had become chronic, the rate of clearance was slow. Those patients who recovered had a quicker rate of clearance and had higher levels of renal function than the potentially chronic patients, who may thus be picked out in the early stages of the disease. If the delay in recovery is due to other causes such as circulatory failure, there is less danger of incomplete recovery from nephritis. Two cases are reported in which chloride deficiency led to serious oliguria, indicating that in these patients the chlorides should be estimated, and if deficient, rectified. Hospital patients with chronic nephritis have probably had the disease for some time before admission, and cannot be considered in a general prognosis of the acute disease. Out of 114 patients with acute early haemorrhagic nephritis 90.5 per cent recovered once the acute stage was over. In the few cases in which the disease became chronic, its progress was slower than usual. The fact that there was no protein restriction in their diet supports the view that protein restriction may retard recovery. The significance of several cases of 'residual albuminuria' after recovery is not clear.

Treatment

Nephrosis

General measures.—C. Wesselhoeft states that, in the treatment of nephritis due to scarlet fever, not only the state of the kidneys but the conditions set up elsewhere in the body must be considered. The kidneys need rest, but this can be carried to extremes in regard to curtailment of both fluids and nutrition. Dehydration should be avoided, and a 5 or 10 per cent dextrose solution intravenously may be indicated in spite of oedema, if the patient refuses liquids or is vomiting, and is the best means of promoting diuresis. Cardiac failure demands digitalis. Fruit juices at first, succeeded later by the addition of milk and cereals, form the accepted diet.

Vitamin A.—G. W. Caldwell obtained favourable results in a case of nephrosis treated with vitamin A and unsaturated fatty acids. Treatment was based on the hypothesis that nephrosis in young children is a deficiency disease in addition to any infective factor. The patient was a girl, aged 7, who had been subject to recurrent oedema of the eyelids and face. The urine had a specific gravity of 1.020, and a heavy trace of albumin. She was going downhill at the time this treatment was begun. She was given 100,000 units of vitamin A daily for 3 days, 80,000 units daily for 2 days, and 60,000 units daily thereafter. In addition 2 teaspoonfuls of

unsaturated fatty acids daily were given; there was then a notable loss of oedema, the weight falling 16 pounds in 4 weeks. A normal diet has since been established.

Nephrotic oedema

Acacia.—A. Goudsmit and M. W. Binger treated 40 adult cases of the nephrotic type of oedema by means of acacia therapy, and all of these, except 4, were promptly relieved of oedema. In most of the unsuccessful cases, failure was due to inability of the patient to take sufficient nourishment and diuretic salts by mouth. A 6 per cent solution of acacia in 0.06 per cent sodium chloride was usually administered. In most cases 500 cubic centimetres of this solution was given in one day, and 45 to 75 minutes were allowed for its administration. The total dosage of acacia given in each course of treatment was limited to 90 to 150 grammes, divided into daily doses of 30 grammes. Diuretic salts are not considered essential, for acacia may produce diuresis when used in conjunction with diet alone. The best results, however, are most likely to be obtained if diuretic salts are included in the regimen.

Caldwell, G. W. (1941) *Arch. Pediat.*, **58**, 247.

Caulk, J. R. (1912) *Trans. Amer. Ass. gen.-urin. Surg.*, **7**, 228.

Gachet, F. S. (1941) *Amer. J. Dis. Child.*, **61**, 1175.

Goudsmit, A., and Binger, M. W. (1940) *Arch. intern. Med.*, **66**, 1252.

Ludbrook, S. L. (1941) *N.Z. med. J.*, **40**, 13.

Randall, A. (1937) *Surg. Gynec. Obstet.*, **64**, 201.

— (1940) *ibid.*, **71**, 209.

Rubin, M. I., and Rapoport, M. (1941) *Amer. J. med. Sci.*, **201**, 734.

Vermooten, V. (1941) *S. Afr. J. med. Sci.*, **6**, 48.

Wesselhoeft, C. (1941) *J. Amer. med. Ass.*, **116**, 36.

Wilson, C., and Byrom, F. B. (1939) *Lancet*, **1**, 136.

— — (1941) *Quart. J. Med. N.S.*, **10**, 65.

NEURALGIA, GLOSSOPHARYNGEAL AND TRIGEMINAL

See also B.E.M.P., Vol. IX, p. 174; and Surveys and Abstracts 1939, p. 445; 1940, p. 423.

Trigeminal Neuralgia

Treatment

Vitamin B₁.—A. S. Rose and B. M. Jacobson treated 4 patients with trigeminal neuralgia by the oral administration of vitamin concentrations and by parenteral injections of vitamin B₁ (thiamin). As controls, 4 other patients with the disease were treated by the intramuscular injection of sterile water. Two of the patients treated with thiamin improved while under treatment, and 2 did not improve. Three of the patients given sterile water improved promptly. The authors conclude that the 5 patients who improved entered on a natural remission of the disease which was not affected by the treatment given, except for the partial psychological relief obtained from constant medical care. Subsequent reports on these 2 patients did not show any essential difference between the condition of those who received vitamin therapy and those who received sterile water. The authors conclude that vitamin B₁ probably has not any specific beneficial effect on trigeminal neuralgia.

Atypical Forms

Superior laryngeal neuralgia

Symptoms and diagnosis.—L. A. Smith, H. J. Moersch, and J. G. Love record 2 cases, in a woman aged 54 years and a man aged 57 years, both successfully treated by resection of the superior laryngeal nerve for this rare form of neuralgia, the first recognized at the Mayo Clinic, and first fully described by Avellis in 1900. The pain is severe, lancinating, paroxysmal and resembling that of tic douloureux, and is usually localized to a small region over the thyrohyoid membrane on one side, from which it may extend to the face as high as the zygoma and perhaps downward to the upper part of the chest. Bilateral cases have been reported. The pain lasts a few seconds to minutes. There is a trigger zone in the piriform sinus of the side affected, and stimulation of the internal branch of the superior laryngeal nerve either at the plica above the piriform fossa or at its entrance to the larynx through the thyrohyoid membrane usually produces an attack. Cocainization of the piriform fossa or anaesthetization of the nerve with procaine hydrochloride at the point where it pierces the thyrohyoid membrane may temporarily prevent an attack. Conditions from which it must be distinguished are: glossopharyngeal neuralgia, if it is not an atypical form of that disease, trigeminal neuralgia, acute cervical fibrositis, and laryngeal nerve anastomoses with the pharyngeal plexus which also receives fibres from the glossopharyngeal nerve; this bears on the relation of superior laryngeal neuralgia to the glossopharyngeal form.

Buccal neuralgia

Clinical picture.—F. L. Reichert states that buccal neuralgia, a form of atypical facial neuralgia, is characterized by a burning, boring, aching, throbbing pain in the lip, cheek, gum, tongue, maxilla, nose, upper jaw, and sometimes the lower jaw, sometimes spreading to the zygoma, into or behind the eyeball, or into the temporal region. An anatomical dissection showed that sympathetic fibres from the carotid sinus followed the arborizations of the facial artery and vein. Extraction of teeth and injection of alcohol into branches of the trigeminal nerve did not give any relief. Tic douloureux of one or more branches of the trigeminal nerve was present in 30 patients with buccal neuralgia. Buccal neuralgia was cured in 5 of

8 patients in whom the cervico-thoracic portion of the sympathetic chain was divided. The condition was relieved in 13 of 17 patients by the simpler procedure of division of the sympathetic fibres with the facial artery and vein at the lower border of the mandible.

Avellis, G. (1900) *Münch. med. Wschr.*, **47**, 1592.

Reichert, F. L. (1940) *Arch. Surg., Chicago*, **41**, 473.

Rose, A. S., and Jacobson, B. M. (1940) *Arch. Neurol. Psychiat., Chicago*, **44**, 1307.

Smith, L. A., Moersch, H. J., and Love, J. G. (1941) *Proc. Mayo Clin.*, **16**, 164.

NEURITIS

See also B.E.M.P., Vol. IX, p. 182; Cumulative Supplement, Key Nos. 1147–1149; and Surveys and Abstracts 1939, p. 446; 1940, p. 424.

Multiple Neuritis

Clinical picture

Acute infective polyneuritis.—B. F. Sampson discusses a group of 10 cases of primary infective polyneuritis among 13 natives of Rhodesia living in a small kraal. There was fever, catarrhal symptoms were conspicuous, and in some cases there was a preceding gastro-intestinal upset. The proximal groups of muscles in the limbs appeared to be at least as affected as the distal. The cells in the cerebrospinal fluid were increased. Death occurred in 5 cases, and was preceded by dysphagia, aphonia, and convulsions. The author suggests the possibility of poisoning with tricresyl phosphate as the aetiological agent.

Guillain-Barré syndrome.—L. Casamajor and G. R. Alpert report on 3 more cases of the Guillain-Barré syndrome in children, a condition characterized by a slowly progressive ascending paralysis of the body, beginning in the lower extremities, with albumino-cytological dissociation of the cerebrospinal fluid, namely increase in protein without an increase in cell count, and a favourable prognosis. The incidence is chiefly in persons between the ages of 20 and 50 years. The onset is generally slow. With the exception of the facial, the cranial nerves are rarely involved. The paralysis is flaccid, with hypotonia, but rarely with atrophy, the involvement being symmetrical, and more profound in the proximal than in the distal muscle groups. The deep reflexes are abolished or markedly diminished, and the superficial reflexes may be absent.

Casamajor, L., and Alpert, G. R. (1941) *Amer. J. Dis. Child.*, **61**, 99.

Sampson, B. F. (1941) *S. Afr. med. J.*, **15**, 23.

NEUROSYPHILIS

See also B.E.M.P., Vol. IX, p. 224; Cumulative Supplement, Key Nos. 1151–1166; Surveys and Abstracts 1939, pp. 154 and 447; 1940, pp. 60 and 425; and p. 102 of this volume.

Intracranial Syphilis

General paralysis of the insane

Combined artificial fever, chemotherapy, and vaccino-therapy.—A. Marin reviews his experience of 2 years' treatment of the forms of neurosyphilis by a combination of artificial fever, chemotherapy, and fever-producing vaccines. He gave artificial fever therapy to 220 patients with 1 death, or 0.4 per cent; these included 137 syphilitics, but also cases of gonorrhoea, chorea, and disseminated sclerosis. These figures are given merely to show the death rate attending this method of treatment. Artificial fever therapy combined with vaccines and chemotherapy (tryparsamide) gave 54 per cent of full remissions in general paresis, and in 7 out of 12 cases of tabes the patients were improved. In the pre-clinical period when there are not any symptoms or signs, except a positive cerebrospinal fluid, the results are generally better than in general paralysis. The immediate serological result in 89 (70 men, 19 women) patients with general paralysis, tabes, tabo-paresis, meningo-vascular, and late non-symptomatic neurosyphilis, showed a fair proportion of cerebrospinal fluids with a marked tendency to become negative. Of the 6 tests made on the cerebrospinal fluid the Pandy, globulin test, and cell count are more rapidly influenced; the Wassermann and Lange gold tests respond more slowly.

Artificial fever and malaria therapy compared.—P. A. O'Leary, W. L. Bruetsch, F. G. Ebaugh, W. M. Simpson, H. C. Solomon, S. L. Warren, R. A. Vonderlehr, L. J. Usilton, and I. V. Sollins evaluate the clinical and serological results obtained in the treatment of general paresis with artificial fever produced by physical methods as compared with malaria therapy. Of the cases reviewed, 1,100 were treated with malaria and 320 with artificial fever. With regard to clinical results, by either method of treatment the earlier in its course the paresis was treated, the more favourable were the results of therapy. The chances of clinical remission in cases of mild paresis were approximately 1 in 2; of intermediate paresis, 1 in 4; and of severe paresis, 1 to 10 in 100. Clinical responses to either type of fever therapy were similar in patients with mild or intermediate paresis on beginning fever therapy. This similarity ceased when treatment was administered to patients with severe paresis, the remission rates for the latter being 1 in 100 with malaria, as compared with 10 in 100 with artificial fever. The crude death rate was higher with malaria (13 per cent) than with artificial fever (8 per cent). The more severe the paresis on beginning treatment with either type of therapy, the higher was the mortality rate. Within each degree of paretic involvement, the crude death rate was higher

under malaria than under artificial fever. Approximately 90 per cent of the total clinical remissions with either method of therapy occurred by the end of the third year of therapeutic observation. None of the patients in whom clinical improvement was delayed until the third year after beginning fever therapy at any time reached the remission stage. Of 432 patients with clinical improvement during the first or second years after beginning fever therapy, 34 per cent of those with clinical improvement the first year and 12 per cent of those with clinical improvement the second year subsequently achieved complete clinical remission. Once a complete remission had been obtained, the chances of its being maintained by either method of treatment were 95 out of 100. In a total of 17 relapses, 15 occurred within three years subsequent to the year of remission. With regard to serological results, the reversal rates for originally positive spinal fluid and blood increased as the duration of therapeutic observation increased. Positive blood reversed more rapidly, though not in greater proportion than positive spinal fluid. The degree of spinal fluid abnormality on beginning fever therapy influenced the proportion of expected reversals. Two-thirds of all the relapses from spinal fluid reversal occurred within one year following the original reversal. Reversals of both blood and spinal fluid were associated more than twice as often with clinical success than with clinical failure. Reversal of the cerebrospinal fluid was more important than reversal of the blood in indicating the chances of complete clinical recovery. The highest percentage of clinical remissions was obtained in patients treated with an average of 69 hours of fever above 101° F. (38.3° C.), of which total fever time 70 per cent was at a level above 105° F. (40.6° C.) with a maximal temperature of 106.9° F. (41.6° C.). Equally good results were obtained in patients treated with an average of 44 hours of fever above 101° F. (38.3° C.), of which total time 57 per cent was above 106° F. (41.0° C.) with a maximal temperature of 107° F. (41.7° C.). The authors believe that fever administered at levels above 106.8° F. (41.5° C.) is unnecessarily risky.

The treatment of 232 patients with general paralysis of the insane during a period of 5 years is the subject of a report by J. R. Ewalt and F. G. Ebaugh. The efficacy of therapeutic malaria and of artificial fever therapy were compared in two groups of patients, who had the same follow-up treatment. Both methods were effective in mild cases but became progressively less effective in severe cases. The artificial fever method showed a superiority of 12 per cent in these cases. Patients who cannot undergo malarial treatment can often be safely treated by artificial fever. The doses generally used were 50 hours of malaria at 104° F. and 50 hours of artificial fever at 105°–106° F. in 10 treatments. Shorter treatment with artificial fever did not alter the results. Careful examination and care after treatment are strongly emphasized. In general the artificial fever method is safer and more effective.

Mental disturbances.—According to A. Gordon, although the usual mental disturbances during the secondary stage of syphilitic infection may be considered with a high degree of certainty as directly due to syphilitic toxins, the same degree of certainty cannot be entertained with regard to a direct relationship of psychosis developed during the tertiary stage. In the former, the mental manifestations are analogous to those observed in toxi-infective states from any cause, and run parallel with secondary manifestations and with fever. In the other cases various psychoses appear many years after the initial infection and they present the typical pictures of classical psychosis, such as Korsakow's syndrome, manic-depressive insanity, melancholia, and dementia paranoides. The author concludes that, at present, no final claim can be made as to a type of mental disease characteristic of syphilis.

Treatment

Prophylaxis

General measures.—In a review of recent advances in the aetiology and treatment of neurosyphilis, Effie L. Hutton concludes with a section on the prophylaxis of neurosyphilis which has not, she states, received the same attention in Great Britain as on the Continent during the last 10 years. The disastrous results of neurosyphilis are many of them degenerative and therefore irreparable if they have once occurred. They can be prevented by avoiding the infection. Further, by timely and sufficient treatment, such as early and adequate administration during primary or secondary syphilis of trivalent arsenic, bismuth, and mercury, the incidence of cerebrospinal syphilis is considerably reduced, though Nonne has contested this view. The examination of the cerebrospinal fluid is essential if the potential neurosyphilitics are to be discovered, and the examination of the cerebrospinal fluid should be as much a matter of routine as the examination of the blood. The writer advocates the adoption of the following routine: every patient with primary or secondary syphilis should be given the usual intensive routine treatment for 2 years; at the end of this time, whether the blood Wassermann reaction is negative or not, a lumbar puncture should be performed; if both blood and cerebrospinal fluid are negative, the patient should be discharged; if the blood is positive and the cerebrospinal fluid negative, further anti-syphilitic treatment should be given; if the cerebrospinal fluid is positive, treatment must be continued until it becomes negative, but pentavalent arsenic or fever therapy must be substituted for trivalent arsenic, bismuth, or mercury. All patients with tertiary or latent syphilis should undergo lumbar puncture before any treatment is started, as the form of treatment required depends entirely upon the cerebrospinal fluid findings.

Iodobismutol and saligenin

With neoarsphenamine or tryparsamide.—G. V. Kulchar, C. W. Barnett, and J. F. Card

report on the use of iodobismutol and saligenin alone or in combination with neoarsphenamine or tryparsamide in 203 cases of neurosyphilis. The therapeutic effect of iodobismutol and saligenin is obtained rapidly and is not increased by prolonged administration. The effect is, however, definitely enhanced by the addition of either neoarsphenamine, or more so by tryparsamide. Iodobismutol with saligenin (a solution of sodium iodobismuthite and sodium iodide in propylene glycol containing saligenin) was given intramuscularly in doses of 2 or 3 cubic centimetres 1 to 3 times weekly.

Tryparsamide and neocryl

Toxicity.—A. O. F. Ross compares the toxicity of tryparsamide and neocryl (sodium succinylmethylamide-*p*-arsonate) in 570 unselected cases of neurosyphilis treated with one or both of these drugs. The drugs were given in equal amounts; 256 patients received tryparsamide and 314 neocryl. A survey of the records of these cases showed that neocryl was in no way inferior therapeutically to tryparsamide, and that toxic effects from its use were much less common. Out of 256 patients treated with tryparsamide, 78 showed toxic manifestations, whereas of the 314 treated with neocryl only 27 showed toxic signs. Both compounds may cause jaundice, dermatitis, and the other undesirable reactions seen after the use of trivalent arsenicals. It is chiefly in its relative harmlessness to the optic nerve that neocryl shows advantage. In 47 of the 78 patients who reacted unfavourably to tryparsamide visual disturbance occurred; in 36 of these the signs were subjective, but in 11 they were objective, 3 of the latter patients becoming totally blind. Neocryl, however, could be held responsible for one case only of visual damage. This occurred in a tabetic patient who unfortunately became suddenly blind. The author concludes that neocryl is preferable in all cases of neurosyphilis in which the administration of pentavalent arsenicals is necessary.

Ewalt, J. R., and Ebaugh, F. G. (1941) *J. Amer. med. Ass.*, **116**, 2474.

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Kulchar, G. V., Barnett, C. W., and Card, J. F. (1940) *Arch. Derm. Syph.*, N.Y., **42**, 46.

Marin, A. (1941) *Canad. med. Ass. J.*, **44**, 161.

O'Leary, P. A., Bruetsch, W. L., Ebaugh, F. G., Simpson, W. M., Solomon,

H. C., Warren, S. L., Vonderlehr, R. A., Usilton, L. J., and Sollins, I. V.

(1940) *J. Amer. med. Ass.*, **115**, 677.

Ross, A. O. F. (1940) *Brit. med. J.*, **2**, 283.

NOSE AND NASOPHARYNX DISEASES

See also B.E.M.P., Vol. IX, p. 256; Cumulative Supplement, Key No. 1168; and Surveys and Abstracts 1939, pp. 90 and 449.

Chronic Obstructive Rhinitis

Treatment

Submucosal injections of sodium psylliate.—E. A. Thacker treated 24 patients with chronic obstructive rhinitis which shrank well with astringents, by the submucosal injection of sodium psylliate. The associated symptoms of headache, sphenopalatine ganglion neuralgia, and post-nasal dripping, were either relieved or markedly improved. Long-standing refractory cases of sinusitis in which there was a chronic engorgement of the turbinates were benefited by this form of therapy. A reduction in the size of the turbinates as well as an improvement in the appearance of the mucous membrane resulted. Before the injection a 2 or 4 per cent butyn solution on two tampons is placed around the turbinates. The tampons are removed, the bevel of the needle is turned away from the long framework of the turbinates, the anterior portion of the mucous membrane is pierced, and the needle is inserted toward the posterior end of the turbinate. As the needle is gradually withdrawn, 0.25 to 0.5 cubic centimetre of a 5 per cent solution of sodium psylliate is injected. A pledget of cotton-wool is then placed in the nose to prevent bleeding from the needle puncture. The cotton-wool is removed after 5 minutes, and a tampon saturated with neosynephrine or ephedrine is placed around the turbinate for 10 minutes. The patient is advised to use a one per cent ephedrine or neosynephrine solution every 2 hours for 5 days. One side of the nose only is injected at a sitting. After 1 week the other side may be treated. Two or three weeks should be allowed before another injection is made into the same tissue.

Sodium morrhuate injections.—E. A. Thacker and G. H. Hauser state that submucosal injections of a 5 per cent solution of sodium morrhuate relieved nasal obstruction in 58 patients with chronic simple, hypertrophic, and vasomotor rhinitis. Associated symptoms, such as headaches, neuralgia of the sphenopalatine ganglion, and post-nasal dripping with chronic symptoms of the upper respiratory tract, were markedly diminished or cured.

Tumours

Juvenile basal fibroma of nasopharynx

F. A. Figi studied 63 cases of juvenile basal fibroma of the nasopharynx at the Mayo Clinic. Of these, 58 occurred in males, and 5 in females. The ages of the patients ranged from 10 to 31. In 45 cases studied in detail, the nasopharynx was involved in all, and the nasal fossae in 34. In a number of cases the antrum, sphenoid, and other accessory sinuses were invaded.

Removal of tissue from these tumours is always attended by profuse bleeding and in some of the more recent cases biopsy was not performed, the diagnosis being based on the history, the age of the patient, the hardness of the tumour, and the characteristic clinical picture. Surgical removal of the tumours involves considerable risk, and recurrences are frequent. The most effective forms of treatment are implants of radium and electro-coagulation supplemented by radium. All the patients in this series who received complete therapy were, at the time of the report, well, except for a boy of 16 who was still under treatment.

Figi, F. A. (1940) *J. Amer. med. Ass.*, **115**, 665.

Thacker, E. A. (1940) *Ann. Otol., etc., St Louis*, **49**, 939.

— and Hauser, G. H. (1941) *Arch. Otolaryngol., Chicago*, **33**, 600.

OEDEMA

See also B.E.M.P., Vol. IX, p. 268; and Surveys and Abstracts 1939, p. 450; 1940, p. 426.

Aetiology

Bilateral oedema of legs

Embarrassment of venous return.—B. Hirsch and R. Ellis report 2 cases of bilateral oedema of the ankles and legs following strapping of the chest wall for fractured ribs. In both cases the oedema disappeared after removal of the strapping. The authors suggest that fixation of the chest wall, by interfering with deep inspiration, ultimately embarrasses the venous return.

Nutritional oedema

Due to jejunocolic fistula.—S. De Navasquez reports a case of nutritional oedema due to a jejunocolic fistula. The patient, a man aged 55, had had a gastro-jejunostomy performed 18 years previously. The oedema extended from the ankles to the clavicles. Blood examination showed a total plasma protein of 4.18 per cent; albumin, 1.82 per cent, and globulin, 2.36 per cent. The oedema was ascribed to the diminished serum albumin, which was well below the normal range of 3.4–4.99. At necropsy a jejunocolic fistula was found, and it was considered that this accessory short-circuit eliminated the opportunity for the absorption of proteins from the small intestine, with resulting depletion of plasma proteins.

Oedema of lung

Associated with menstruation.—J. Edeiken and J. A. Griffith, Jun. report a case of cyclical pulmonary oedema associated with the menstrual periods of a young woman with advanced mitral stenosis. Attacks of pulmonary oedema occurred during 14 successive menstrual periods. Injections of mercupurin intravenously before the menstrual period prevented oedema during 3 periods, but a hacking cough and tightness of the chest occurred. The patient became entirely free from pulmonary symptoms following irradiation of the pituitary gland.

De Navasquez, S. (1941) *Brit. J. Surg.*, **28**, 468.

Edeiken, J., and Griffith, J. A., Jun. (1941) *J. Amer. med. Ass.*, **115**, 287.

Hirsch, B., and Ellis, R. (1940) *Brit. med. J.*, **2**, 593.

OEDEMA, HEREDITARY

See also B.E.M.P., Vol. IX, p. 282; and Surveys and Abstracts 1939, p. 450; 1940, p. 427.

Clinical Picture

Persistent oedema of the legs

Incidence in a family.—W. L. P. Dassanayake describes a family with several examples of persistent hereditary oedema of the legs. The father and mother were quite normal, whereas of 5 children, the middle 3, all males, were affected. In the second generation all the children, both males and females, of the affected parents shared the familial condition. The third generation have so far escaped. In external appearance the condition is very similar to elephantiasis of the legs, except that several members of the same family have had the condition from birth.

Dassanayake, W. L. P. (1940) *J. trop. Med. (Hyg.)*, **43**, 221.

OEESOPHAGUS DISEASES

See also B.E.M.P., Vol. IX, p. 287; Cumulative Supplement, Key Nos. 1176–1188; and Surveys and Abstracts 1939, pp. 43 and 450; 1940, p. 427.

Congenital Malformations

Congenital atresia

In an infant.—M. I. Ealing records a case of congenital atresia of the oesophagus in a male infant, fatal on the fifth day of life. The upper two-thirds came to an end in a blind pouch, and there was, as usual, a fistula between the lower part and the trachea. From a review of some other reported cases it seems probable that sometimes the condition is regarded as merely broncho-pneumonia because cyanosis is constant and aspiration pneumonia extremely prone to occur. Life is seldom prolonged beyond the seventh day of life, but in 2 cases survival lasted for 98 and for at least 42 days; these were recorded by Leven, who described a new two-stage operation of gastrostomy of the exteriorized stomach, followed later by cervical oesophagostomy and ante-thoracic oesophagoplasty, which was carried out in these 2 patients.

It is, however, concluded that operative treatment is not likely to be very successful, on account of the rapidity with which pulmonary infection becomes established.

Ealing, M. I. (1940) *Brit. med. J.*, 2, 83.

Leven, N. L. (1936) *J. thorac. Surg.*, 6, 30.

OPHTHALMOPLEGIA

See also B.E.M.P., Vol. IX, p. 315.

Chronic Progressive Ophthalmoplegia

Exophthalmic type

H. G. McGregor describes a case of exophthalmic ophthalmoplegia in which the ophthalmoplegia was present for long before the onset of severe ophthalmos. This tends to disprove the conception that the ophthalmoplegia is the result of a rapidly produced exophthalmos. That the condition is an entity distinct from toxic goitre is apparent from the higher age incidence, the preponderance of males, and the fact that thyrotoxicosis does not play any part in the disorder. It differs from myasthenia gravis complicating thyrotoxicosis in that the paralysis is limited to the ocular muscles, fatiguability is absent, and there is not any response to prostigmin.

McGregor, H. G. (1940) *Lancet*, 2, 579.

OVARY DISEASES

See also B.E.M.P., Vol. IX, p. 318; Surveys and Abstracts 1939, p. 451; 1940, p. 428; and p. 21 of this volume.

Tumours

Aetiology and classification

Incidence, symptomatology, and prognosis.—M. B. Dockerty analyses 75 cases of the more recently recognized primary ovarian tumours and summarizes them as follows: (1) Granulosa-celled growths forming 60 per cent of the cases of the total; precocious menstruation, early development of secondary sex characters, feminization, post-climacteric menstruation; unilateral in 95 per cent with survival after removal for 5 years in 95 per cent. The hormone elaborated is oestrogen. (2) Theca-celled growths from the theca of follicles, forming 12 per cent of the total; post-menopausal in 80 per cent; post-climacteric bleeding; unilateral in 100 per cent; 5-year survival in 75 per cent, the hormone elaborated being oestrogen. (3) Arrhenoblastomas, derived from testicular rests forming 3 per cent of the total; the symptoms were sterility, hirsuties, atrophy of the breasts, hypertrophy of the clitoris, voice changes, amenorrhoea, masculinization; unilateral in 100 per cent; 5-year survival in 75 per cent. The male sex hormone is elaborated. (4) Dysgerminomas, arising from undifferentiated sex cells and containing giant cells, forming 12 per cent of the total; unilateral in 65 per cent; 5-year survival in 60 per cent; pseudo-hermaphroditism; hypoplasia of genitalia; no hormone secreted. (5) Brenner tumours derived from embryonic rests or teratomas occurring after the menopause in 70 per cent, forming 13 per cent of the 75 tumours analysed; unilateral in 95 per cent; benign; no hormone secreted.

Clinical types

Malignancy and secretion.—M. B. Dockerty gives some further statistics, based on 500 cases at the Mayo Clinic. Of all ovarian tumours 80 per cent are cystic and 20 per cent solid. Of the latter 63 per cent are malignant. In addition, 15 per cent of the solid tumours are 'functioning', namely produce hormones and give rise to special clinical symptoms on the basis of altered physiological processes. Of the non-functioning solid tumours, adenocarcinoma headed the list (41 per cent), followed by fibroma (33 per cent) and Krukenberg's metastatic tumour (10 per cent).

Traumatic rupture of ovarian dermoid cyst.—M. C. Piper records 2 cases of rupture of a benign ovarian cyst. In one of these laparotomy showed the peritoneal cavity to be almost entirely obliterated by dense fibrous adhesions between the parietal and the visceral surfaces, and many tubercle-like nodules were present and suggested tuberculous peritonitis. A study of immediate frozen sections, however, proved this view to be wrong, and showed foreign-body granulomas containing fat droplets, and it was suggested that this might be due to rupture of an ovarian dermoid cyst; this was found to be the case. The foreign-body reaction to fat was similar to that described by D. H. Donath as due to the introduction of various mineral oils into the abdominal cavity to prevent post-operative adhesions. Reference is made to J. M. Marshall's collection of 415 cases of ovarian dermoid cysts; rupture of a benign ovarian cyst is said to be rare.

Primary signet-ring cell carcinoma

W. Schiller and D. D. Kozoll report a case of primary signet-ring cell carcinoma of the ovary in an obese woman, aged 61, who had a primary growth in the right ovary with numerous intra-abdominal metastases. The authors give an account of the tumours which Krukenberg (1895) described as characterized by the presence of signet-ring cells and erroneously named *fibro-sarcoma ovarii mucocellulare carcinomatodes*; these tumours were subsequently shown to be bilateral metastatic tumours secondary to primary carcinoma of the gastro-intestinal tract. There remain, as in the authors' case, cases of signet-ring carcinomas primary in the ovary, the so-called primary Krukenberg tumour, better designated as primary

signet-ring carcinoma of the ovary. Of these primary ovarian growths there are on record 9 authentic and 2 doubtful examples.

Teratomas

Malignant dermoid cyst.—M. Smeltzer reports 2 cases of a solid teratoma, one in the ovary of a girl aged 8, and the other in a girl aged 14. Both patients received X-irradiation, and in both there was clinical evidence of recurrence of the tumour before X-ray therapy was given. There was not any evidence in either case that X-rays had any effect on the growths, and the author therefore questions the efficacy of deep X-ray therapy in this type of growth. Such cases should, however, be given X-ray therapy in therapeutic doses immediately after the primary operation.

Granulosa and theca-celled tumours

D. N. Henderson surveys the granulosa and theca-celled tumours of the ovary which, first described by von Kahliden in 1895, later in 1915 by Robert Meyer, did not arouse much interest until it was shown that they secreted oestrin and were feminizing tumours. Although more than 250 cases have been reported, this does not give a true picture of their incidence, as their pathological nature has become widely recognized in recent years only. Among Henderson's 612 ovarian tumours the incidence was 2.6 per cent. It is difficult to estimate their malignancy; three histological types have been described, the follicular or mature, the cylindroid, and the sarcomatoid (Meyer). Among 54 cases 15 per cent were clinically and microscopically malignant (Traut and Marchette), but Henderson had not seen a case. In size the tumours vary from those of quite small size to those weighing 34 pounds; the size does not appear to bear any relation to the hormonal activity. The oestrin causes hyperplasia of the endometrium, myometrium, and in some cases the breasts and external genitals, and during the years of sexual maturity, periods of amenorrhoea alternating with irregular, prolonged, or profuse haemorrhage. Before puberty the tumours cause precocious menstruation, and secondary sex characters. If after an established menopause uterine bleeding recurs and the uterus enlarges, cancer of the uterus or cervix is a more probable cause than granulosa-celled tumour of the ovary. Reference is made to the observation of J. Furth and J. S. Butterworth that irradiation may be followed in mice by granulosa-celled ovarian tumours; this bears on the possible risk of X-rays in women.

Treatment

Carcinoma of the ovaries and tubes.—R. E. Fricke states that, for carcinoma of the ovaries and tubes, the treatment of choice is operation, whenever possible. If the condition is inoperable, palliative radium therapy given intravaginally and high-voltage X-ray therapy prove of help. If, however, the risk of operation is not too great, the treatment of choice is surgical excision followed by the vaginal application of radium and by X-ray therapy. Carcinoma of the uterine fundus is generally of a low grade, is confined within the thick muscular wall, metastasizes slowly and is thus favourable for treatment. Post-operative irradiation is valuable in the prevention of recurrence. Carcinoma of the cervix, which is four times more frequent than carcinoma of the fundus, is more of a radiological problem, as it can be more readily watched and more easily treated. Immediate treatment by radium and X-rays is indicated. Primary carcinoma of the vagina, fortunately rare, is a high-grade squamous-celled carcinoma which spreads and metastasizes rapidly.

Dockerty, M. B. (1941) *Proc. Mayo Clin.*, **16**, 91 and 104.

Donath, D. H., in press.

Fricke, R. E. (1941) *Proc. Mayo Clin.*, **16**, 93.

Furth, J., and Butterworth, J. S. (1936) *Amer. J. Cancer*, **28**, 66.

Henderson, D. N. (1941) *Canad. med. Ass. J.*, **44**, 20.

Marshall, J. M. (1928) *Proc. Mayo Clin.*, **3**, 4.

Piper, M. C. (1941) *Proc. Mayo Clin.*, **16**, 349.

Schiller, W., and Kozoll, D. D. (1941) *Amer. J. Obstet. Gynec.*, **41**, 70.

Smeltzer, M. (1941) *Amer. J. Obstet. Gynec.*, **41**, 616.

Traut, H. F., and Marchette, A. A. (1940) *Surg. Gynec. Obstet.*, **70**, 632.

PAIN

See also B.E.M.P., Vol. IX, p. 359; Surveys and Abstracts 1939, pp. 19 and 454; 1940, p. 429; and p. 88 of this volume.

Measurement of the Thresholds for Pain

R. M. Wilder, Jun. reports the results of an examination of 394 patients, unselected except for the avoidance of those with known moderate to severe hypertension. E. Libman described a test for a rough estimate of thresholds for pain, namely by pressing firmly on the styloid process of the mastoid; this method is not entirely satisfactory because the amount of pressure cannot be quantitatively evaluated. E. Hollander described a more accurate plan which was utilized by Wilder. The apparatus used is the cuff of an ordinary mercurial sphygmomanometer, on the surface of which a piece of roughened metal, such as that used in food graters, is attached. When the cuff is inflated, the level of sensitivity is indicated by the point on the mercurial scale at which the patient first shows evidence of distress by wincing, by changing expression, or sometimes by crying out. The nearest 10 millimetres of mercury mark on the mercurial manometer when such a reaction occurs, is taken as the pain point. This modified

sphygmomanometer cuff can be used for taking the blood pressure, and it is rather surprising that the discomfort did not as a rule cause much rise of the blood pressure. The average pain threshold among the males was 181 millimetres of mercury and among the females 122 millimetres of mercury. Careful analysis of the age groups did not show particular differences. Obesity did not seem to increase the sensitivity of the skin to pain; in a group of obese women the sensitivity levels were on average slightly higher than for all women, and the same held good for a group of obese men. Among patients with functional disease the pain sensitivity threshold was significantly lower than that of those with organic disease.

Hollander, E. (1939) *J. Lab. Clin. Med.*, **24**, 587.

Libman, E. (1934) *J. Amer. med. Ass.*, **102**, 335.

Wilder, R. M., Jun. (1940) *Proc. Mayo Clin.*, **15**, 551.

PANCREAS, DISEASES

See also B.E.M.P., Vol. IX, p. 386; Cumulative Supplement, Key Nos. 1203–1208; and Surveys and Abstracts 1939, p. 455; 1940, p. 430.

Inflammatory Conditions

Acute haemorrhagic pancreatitis

Complicated by diabetes mellitus.—H. B. Shumacker reports a case of severe diabetes mellitus developing during the course of acute haemorrhagic pancreatitis. Reviewing the subject, he points out that glycosuria occurs in about 11 per cent of patients with acute pancreatitis, and that hyperglycaemia and decreased glucose tolerance occur in a much higher proportion of cases. Diabetes mellitus may develop during acute pancreatitis. It may terminate rapidly in coma, or the patient may survive with a persistent diabetes of greater or less severity. It may ensue after a few months or many years. At least 2 per cent of all patients with severe acute pancreatitis acquire diabetes mellitus, and of those surviving the acute illness, from 3 to 10 per cent become the subjects of diabetes mellitus. A much larger percentage of surviving patients show milder grades of altered carbohydrate metabolism. In mild cases of acute pancreatitis diabetes is unlikely to follow.

Calculi

Diagnosis

S. R. Townsend reviews the subject of pancreatic calculi and reports 3 cases to illustrate some of the difficulties in its diagnosis from conditions such as cholecystitis, gall-stones, and calculi in the right kidney. It is somewhat rarely recognized. In 1925 S. J. Seeger collected 100 cases and since that date the number has been more than doubled, and with the routine use of X-rays it is probable that the incidence will continue to increase. In the past, 65 per cent of the cases were recognized at necropsy and 35 per cent at laparotomy. It most commonly occurs between 30 and 40 years of age, and is three times commoner in males than in females. In diabetes mellitus it occurs in 3 per cent of cases, and 'painful diabetes' should suggest calculi. Oedema of the head of the pancreas, due to calculi, may compress the common bile-duct and cause jaundice. Radiological examination is the most reliable means of diagnosis, but there may be difficulties with calcified lymphatic glands, biliary and renal calculi. Operative removal is the only form of treatment; but the surgical mortality is 17 per cent.

Cysts

Signs and symptoms

H. B. Martin reports the case of a Hindu boy, aged 11 years, taken acutely ill with intermittent pain, vomiting, a temperature of 100° F. rising to 101.4° F., and a pulse of 120 reaching 140. There was an oval lump, about half the size of his head, extending downwards from the right costal arch; it was tender, dull on percussion, tense, and slightly movable. The rest of the abdomen was not tender or 'boarded'. There was a history of a worm having been passed, but the faeces did not contain any ova. The leucocyte count was 20,000 per cubic millimetre. Laparotomy showed an obviously cystic lump, with innumerable loculated thin-walled cysts in the head of the pancreas; the cysts varied in size from that of a pea to that of an egg; some contained clear fluid, others altered blood, bile, and necrotic material. As many as possible were aspirated so that the head of the pancreas became, as it were, deflated. A drain was inserted in the right loin, the wound closed, and several injections of soluseptasine given as a protection against suppurative. Complete recovery was the result. The explanation of events appears to be haemorrhage into, and inflammation of, the head of the pancreas, already the site of cystic disease.

Tumours

Carcinoma of head of pancreas

S. C. Franco reviews 40 cases of carcinoma of the head of the pancreas with a view to determining clinical indications which would lead to earlier diagnosis. The author considers that the disease should be suspected in cases in which malignancy is probable, but X-ray investigation of the gastro-intestinal tract is negative or dubious. A change in the intestinal picture in the presence of abdominal pain may give a lead. Loss of weight is often severe, jaundice is not always present. An enlarged liver and gall-bladder are the most common abdominal findings. Achlorhydria is present in about 25 per cent of cases. Sugar in the urine or a raised blood pressure may be an indication in some cases.

General Diseases**Diagnosis**

Secretin test.—J. S. Diamond and S. A. Siegel discuss the value of the secretin test in the diagnosis of pancreatic disease in 80 patients and in 24 normal subjects. The test consists of the intravenous injection of 0.75 milligram of secretin per kilogram body weight; this causes a considerable increase in the flow of pancreatic juice; the use of a double-lumen gastro-duodenal tube provides a clear uncontaminated juice rich in bicarbonate and enzymes. In severe lesions of the pancreas all functions are simultaneously involved, and become greatly diminished. In milder forms the enzyme production is the first to suffer. The test supplies valuable information concerning disturbed function of the pancreas in chronic states hitherto unrecognized.

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PARALYSIS AGITANS

See also B.E.M.P., Vol. IX, p. 408; Surveys and Abstracts 1939, p. 458; and p. 5 of this volume.

Treatment**Quinine**

A. T. Milhorat found that quinine reduced muscular rigidity in several patients with paralysis agitans, and often relieved muscular pain. These effects gradually diminished after the drug had been taken for some weeks. After the drug had been discontinued for a few weeks, its renewed administration was generally followed by effects on muscular rigidity. Prostigmin methylsulphate increased muscular stiffness and tremor in paralysis agitans. Atropine and scopolamine abolished and prevented these effects of prostigmin methylsulphate.

Vitamin B₆

A. B. Baker reports on the treatment of 15 patients with paralysis agitans by injections of pyridoxin hydrochloride (vitamin B₆). Nine of the patients had idiopathic or arteriosclerotic parkinsonism, and of the remaining 6, 3 had post-encephalitic paralysis, 1 had a syphilitic form, and in 2 cases the causes were unknown. Intravenous injections of 50–100 milligrams were given daily for from 2 to 4 weeks and supplemented in most cases by brewers' yeast taken orally. Four patients of the idiopathic group and 1 of the post-encephalitic group showed moderate or definite improvement. One of the former group with senile chorea showed remarkable improvement. Four additional patients of the idiopathic group were given pyridoxin orally but only 1 of these showed noticeable improvement. Age and the duration of the disease do not affect the results of treatment.

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PARATHYROID GLAND DISEASES

See also B.E.M.P., Vol. IX, p. 424; and Surveys and Abstracts 1939, p. 459; 1940, p. 432.

Hypoparathyroidism**Parathyroid tetany**

Complicated by psychosis.—J. A. Greene and L. W. Swanson found psychosis as a complication of parathyroid tetany in 5 out of 18 cases. The psychical disturbances are generally of the toxic delirium type, occurring during the first few months, and may be the only obvious manifestation of tetany. The prognosis is good, and the condition is not likely to recur although the parathyroid deficiency may relapse. The response to adequate treatment is slower than are the other manifestations of tetany, and 3 or 4 weeks, or several months, may elapse after adequate control of the tetany before the psychosis subsides.

In pregnancy.—G. F. Kowallis records a case of spontaneous parathyroid insufficiency in a woman, aged 32 years, during and after her second pregnancy, the whole of the first pregnancy having been passed through normally under calcium treatment. A search through the records of the Mayo Clinic showed the rarity of this condition—a total of 10 other cases. In the second pregnancy calcium was not given until after the onset of symptoms of hypoparathyroidism—nausea, vomiting, and otherwise unexplained collapse of the lower extremities. Later, about the sixth month of pregnancy, the patient noted numbness and tingling of the hands when at rest, and cramps in the legs two or three times at night. About 6 weeks after delivery convulsions first appeared, and occurred at intervals of 2 weeks, the patient then being admitted to the Mayo Clinic. Physical examination, including that of the central nervous system, gave negative results, except for personality changes, such as irritability, stubbornness, and forgetfulness, which appeared after the onset of the fits, and strongly positive Chvostek's and Trousseau's signs. All laboratory investigations, including radiological examination of the skull, gave negative results except the low serum calcium of 5.1 milligrams per 100 cubic centimetres and the high serum phosphates of 4.8 milligrams per

100 cubic centimetres. The Sulkowitch reaction was negative at first, but later with general improvement became positive. This test is a help in the determination of the dosage of calcium salts and of dihydrotachysterol; equal parts of the reagent are added to the urine and the calcium comes down as a fine white precipitate of calcium oxalate; absence of precipitate means absence of calcium in the urine and a serum calcium of 5 to 7.5 milligrams per 100 cubic centimetres. If the precipitate looks like milk, there is excess of calcium in the urine and danger of hypercalcaemia exists; if there is a fine white cloud the calcium level is within normal limits. The electro-encephalogram showed atypical cerebral dysrhythmia. Treatment at the outset was calcium lactate 3 teaspoonfuls (12 cubic centimetres) 4 times daily and dihydrotachysterol (A.T. 10) 1 cubic centimetre daily, the dosage of the drugs being controlled by the Sulkowitch test. The improvement of the patient under this treatment in 3 weeks was dramatic; she went home with instructions for continued treatment and returned twice for examination and remained well. The treatment of hypoparathyroidism has been much improved by Holtz's introduction in 1934 of dihydrotachysterol, a photochemical derivative of ergosterol.

Hyperparathyroidism

Clinical features

Condition of mouth.—M. S. Strock describes dental symptoms arising from hyperparathyroidism. Forty-five patients were observed, all showing some of the following signs: visible or palpable tumours of the jaws; mal-occlusion or distortion of the normal teeth arrangement; cyst-like cavities of the jaws; diminished dental caries; osteoporosis; closely meshed trabeculae and the absence of the lamina dura. In spite of drastic withdrawals of calcium and phosphorus from the blood the teeth remain well calcified and radiologically appear opaque, thus calcium deposits in the teeth cannot be reabsorbed into the blood. The signs mentioned above should be carefully watched as they may herald the onset of hyperparathyroidism.

Clinical types

Spinal osteoporotic type.—According to E. A. Merritt and R. M. Caulk, the spinal osteoporotic type of hyperparathyroidism occurs most often in women past the menopause. The chief complaint is intense pain in the back, which is constant, aggravated by movement, and is often worse when the patient is lying down. There is an associated profound asthenia and loss of weight. Skiagraphy shows advanced mineral deficiency of the bone with collapse of the bodies and typical 'fish-tail' appearance of the spine. Kyphosis and scoliosis are present in varying degree.

Morbid anatomy

Complicated by prolonged renal insufficiency.—R. S. Downes and V. Scott report a complicated case of the interrelations of the parathyroids and the kidneys, the like of which has not, as far as they can ascertain, been previously described. A man, aged 50 years, had had renal colic due to calculi 20 years earlier, and in 1938 was found radiologically to show mottled areas of increased density scattered over both kidneys, decalcification of the skeleton, hypertension, and moderate albuminuria, with specific gravity of the urine 1,008. This raised the question of hyperparathyroidism. There was, however, no further evidence of a parathyroid adenoma, the serum calcium and phosphorus values not lending any support to such a diagnosis; it was decided that an exploratory operation for a parathyroid adenoma was not advisable. Six months later the patient came under observation again with severe anaemia and evidence of uraemia, and became comatose, dying with a temperature of 107° F. At the necropsy one of the parathyroids contained a cystic adenoma. The kidneys weighed 100 and 120 grammes, showed a nodular cystic surface, diffuse calcinosis, and histologically most of the glomeruli showed hyaline change or extreme thickening of Bowman's capsules; there were numerous calcified areas. It thus became clear that the patient had been the subject of hyperparathyroidism, and it was suggested that the apparently contradictory chemical changes of calcium and potassium could be explained by the effect of prolonged renal insufficiency acting as a complication of primary hyperparathyroidism.

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PAROTID GLAND DISEASES

See also B.E.M.P., Vol. IX, p. 449; Cumulative Supplement, Key Nos. 1217-1226; and Surveys and Abstracts 1939, p. 461; 1940, p. 434.

Mixed Tumours

Treatment

Total parotidectomy.—Hamilton Bailey reports 6 cases of total removal of mixed parotid tumours and recommends total surgical excision rather than deep X-rays, especially as most of these tumours are radio-resistant. Some statistics give a mortality percentage as high as 30, most of them, according to R. Kennon, within the first year. Other reasons for the reluctance to operate on parotid tumours are section of the facial nerve and the production of a salivary fistula. Bailey points out that the surgical anatomy of the parotid should be

Pemphigus Solitarius Cicatrisans*Clinical picture*

T. Davies describes a condition which he calls 'pemphigus solitarius cicatrisans'. It is characterized by bullae occurring, generally singly, at intervals varying from two days to two years. The bulla, which is often preceded by an erythematous nodule or ring, has thick walls, and may last several days without the contents becoming turbid. It is followed by an ulcer with thickened, torpid edges, taking many weeks to heal, and invariably leaving a scar. The lesions occur on skin which is otherwise normal, and are mainly on the hands and wrists.

Pemphigus Neonatorum*Aetiology*

Carrier of infection.—S. D. Elliott, E. H. Gillespie, and E. Holland report an outbreak of skin infection resembling pemphigus neonatorum in a nursing home. Twenty-two infants, 2 mothers, and 1 nurse were affected. Profuse, almost pure, cultures of *Staphylococcus pyogenes* were obtained from the lesions in 10 out of 11 cases examined bacteriologically, and all belonged to Type IIIc (Cowan). A nurse who had two lesions was found to be a nasal carrier of staphylococci of the same type. Staphylococci of the same type were also recovered from plates exposed to the air during the outbreak in two wards in which were infected patients, and in the nurses' dining-room. Investigations proved that these organisms were not isolated from the air of two unoccupied wards, or from a ward containing an uninfected patient. The evidence suggests that the nurse may have been the source and also the means of spreading infection.

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Lever, W. F., and Talbott, J. H. (1941) *Arch. Derm. Syph., N.Y.*, **43**, 341.

PENIS AND SCROTUM DISEASES

See also B.E.M.P., Vol. IX, p. 498; and Surveys and Abstracts 1939, p. 465; 1940, p. 437.

Penis*Cancer*

Radium therapy.—M. Lederman reports 28 cases of cancer of the penis treated by radium at the Royal Cancer Hospital, London, between 1929 and 1939. The results obtained by the different radium procedures employed are mentioned. Including all techniques of treatment, the results obtained were 53.8 per cent of 5-year cures and 61.9 per cent of 3-year cures.

Scrotum*Tumours*

Haemangioma.—T. L. Schulte reports the twenty-first recorded case of haemangioma of the scrotum. On account of proximity of the testes surgical excision rather than X-rays, radium or carbon dioxide snow is usually the treatment of choice. Further, redundancy of the scrotal skin facilitates excision and helps in obtaining satisfactory closures of the wound. The patient was a boy, aged 3 years, with a haemangioma of the right side of the scrotum and similar tumours in the right lower limb. These tumours, which are usually congenital, were divided by T. E. Gibson into (a) those of the skin, and (b) those of the subcutaneous tissues and usually unilateral, but may involve the superficial tissues of the penis and under surface of the thigh. They may be confused with varicocele, but their position in the wall of the scrotum should make differential diagnosis fairly easy.

Penis and Scrotum*Elephantiasis*

Surgical treatment.—E. de Savitsch states that the only satisfactory treatment for elephantiasis of the scrotum and penis is surgical, and that its success depends largely on mobilization of sufficient healthy skin to permit construction of a new scrotum. The operation is carried out under spinal anaesthesia. The surgical technique for removal of elephantiasis of the penis is simple; all that is necessary is to make a circular incision slightly beyond the border of the healthy tissue, and subsequently to pull off the diseased skin together with the underlying gelatinous layer. The area is then covered by vaseline gauze, and then by a layer of oilcloth. Within a short time granulation tissue covers the area, and there is proliferation of epithelium from the border of the healthy skin. The first consideration in the surgical treatment of elephantiasis of the scrotum is haemostasis. The scrotum is transfixed by a hook and lifted on a pulley to a right angle to the plane of the body. A tourniquet is placed as close as possible to the neck of the mass. The size of the flap of skin needed to cover the penis is determined, and detached from the mass. The large blood vessels which supply the mass are found, and tied as high as possible in the inguinal region, where they are ligated and cut. The mass is bisected and cut at the perineal end of the two newly constructed scrotal flaps.

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PEPTIC ULCER

See also B.E.M.P., Vol. IX, p. 504; Cumulative Supplement, Key Nos. 1236 and 1237; and Surveys and Abstracts 1939, pp. 46, 167, and 466; 1940, pp. 5, 12, 25, and 437.

Peptic Ulcer of Stomach and Duodenum*Aetiology*

Effect of nicotine on gastric acidity.—I. Ehrenfeld and M. Sturtevant, investigating the effect of smoking tobacco on gastric acidity, found that a significant increase in acidity followed smoking under certain test conditions. This increase was slightly greater in patients with peptic ulcer than in a control group. It appears to be more marked with the use of untreated cigarettes than after smoking cigarettes from which part of the nicotine had been removed.

Age influence.—F. W. Muslow, studying the incidence of death in peptic ulcer in elderly patients, found that about one-third of these occurred in persons over the age of 60, about one-third in the sixth decade, and the remainder under 50 years of age. A review of the reported cases showed that massive haemorrhage was nearly twice as frequent as perforation in patients over the age of 40. About 10.5 per cent of 4,079 patients with peptic ulcer were above this age.

Histamine factor.—The hypothesis that histamine is a factor in the production of peptic ulcers and the use of histaminase in the treatment of ulcers, led H. Necheles, W. H. Olson, and W. Scruggs to experiment with both drugs on gastric secretions in dogs with Pavlov pouches. After regular doses of histamine a constant flow of gastric juice was obtained which was not diminished by histaminase either alone or after a meat meal. Similarly pancreatic, salivary, and biliary secretions were not decreased. In many animals there was even a general increase in the secretions. Gastric motility was unaffected by histaminase. Variations in the responses to histaminase, even by the same dogs, indicates that the commercial histamine may contain other, perhaps non-specific, substances.

Pathology and morbid anatomy

Perforation of tuberculous duodenal ulcer.—A. B. Beresford-Jones records an extremely rare condition, perforation of tuberculous ulceration of the third part of the duodenum into the aorta. Ulceration, simple or tuberculous, in the third part of the duodenum is extremely rare; the author refers to two records of tuberculous ulcer of the duodenum. The case recorded now was that of a woman, aged 53, with several attacks of gastro-intestinal haemorrhage, tentatively diagnosed as carcinoma of the stomach. At laparotomy a number of nodules on the peritoneum were seen; these were later found to be tuberculous. On the ninth post-operative day the patient fainted, on the twelfth post-operative day she passed a blood cast 12 inches long, and on the next day she was very ill and died. A partial necropsy brought to light perforation of the aorta with blood-clot into the third part of the duodenum, surrounded by adhesions. Microscopical examination showed that the nodules and the tissues round the perforation led to the most probable explanation as a tuberculous pre-aortic lymphatic gland becoming adherent to the aorta and duodenum and rupturing into both for one-third of an inch in diameter. Although this fistula was occupied by a firm clot, the stomach and intestines were distended with blood. The peritoneum, great omentum, and pleura showed tubercles. The intestinal tract was free from other tuberculous ulcers. There was considerable sclerosis of the aorta.

Clinical picture

Simultaneous perforations.—G. H. Stobie places on record a case of perforations of large and indurated ulcers found at laparotomy, both on the lesser curvature of the stomach, high up, and on the anterior surface of the duodenum, $1\frac{1}{2}$ inches from the pylorus; the perforation of the gastric ulcer admitted the little finger, that of the duodenal ulcer was quite small. The patient, a farm labourer aged 18 years, had had symptoms of peptic ulcer for two months, though the character of both ulcers pointed to a longer duration. The author failed to find a report of a similar case.

Peptic ulcer in childhood.—O. M. Moore of Vancouver records 8 cases of peptic ulcer, all but one duodenal, in children (boys 6, girls 2) between the ages of 6 and 14 years. These were all detected after January 1939, not, it is stated, because the occurrence has become more common but as the result of more attention to its diagnosis, especially radiological examination. Before 1939 the youngest patient with peptic ulcer at the hospital was seventeen years of age. Peptic ulcer in childhood has been regarded as very rare; reference is made to H. B. Kellogg's estimate that the total number of recorded cases up to 1939 was 36 only. Clinical diagnosis is difficult, especially in patients under the age of ten years, because these children are inaccurate in their description and localization of pain, and are specially susceptible to leading questions. In 2 cases the father gave a history of peptic ulcer; in 3 children the pain was so severe as to suggest acute appendicitis. In 7 cases the pain was localized in the epigastric and para-umbilical regions. Abdominal tenderness in these regions was present in 6 children. In 2 children there were complications, severe and rather persistent tarry stools in one, and in the other a moderate degree of stenosis shown by radiological examination but not by untoward symptoms. Six patients were put on a modified Meulengracht diet and the other 2 on a bland diet serving the same purpose.

Treatment

Partial gastrectomy.—E. B. Lewis and R. G. Lemon analyse 212 consecutive cases, most of them during the last 5 years, in which partial gastrectomy of a third or more of the stomach

was performed at the Mayo Clinic for duodenal ulcer. The chief advantage of this Polya operation over gastro-enterostomy, such as Billroth type 1, is that there is a greater lowering of gastric acidity in a higher percentage of cases. Post-operative death occurred in 4 cases, and of the remaining 208 patients 197, or 95 per cent, were followed up, and of these 83.5 per cent were well, 14 per cent required some restriction of diet and activity to keep well, and 2.5 per cent showed evidence of anastomotic jejunal ulcer. The best results were obtained among the 43 cases in which there was a gastric as well as a duodenal ulcer; of 38 such patients followed up 92 per cent were well and 8 per cent required some post-operative care.

Gastric resection and acidity.—In a preliminary survey, M. T. Friedell considers the influence of more extensive partial resection of the stomach on the production of anacidity and so on the treatment of duodenal ulcer. At the Mayo Clinic 114 patients were divided into two categories: those who had undergone resection of (1) half and (2) more than half of the stomach, and compared as regards the production of anacidity. Group (1), of more extensive gastric resection, showed an increment of only 2.5 per cent of a possible approximate 25 per cent of anacidity that might be anticipated if the degree of anacidity ran parallel with that of resection. The conclusion is reached that patients who are confirmed 'ulcer formers', as evidenced by previous perforated duodenal ulcers, in spite of high gastric resection do not readily show gastric anacidity.

Vitamin A (avoleum).—S. F. Seelig reports the results of the treatment with vitamin A (avoleum) of 13 cases of chronic gastric ulcer, selected as having been resistant to medical treatment. The patients had been ill for more than a year with the disease as shown radiologically, by gastroscopy whenever possible, and clinically. In 11 out of the 13 (9 males, 4 females) patients no other form of treatment was given. Approximately 4 or 5 weeks after beginning treatment, which was ambulant and did not include prohibition of smoking or alcohol, all the patients, except one with an hour-glass stomach and one other, were free from pain, and showed uniform clinical improvement from 7 to 14 days after the start of treatment. Experimental and clinical observations are given, suggesting that vitamin A deficiency may be responsible for gastric ulceration.

Aluminium hydroxide.—S. A. Wilkinson and P. D. Comanduras report on the neutralizing effects of the Sippy powders and of aluminium hydroxide in reducing gastric acidity, during 2 years. After the use of aluminium hydroxide, 40 per cent of the acid determinations at the end of 3, 6, 9, and 12 months showed a reduction in gastric acidity of 20 units or more. After the Sippy powders only 20 per cent of the determinations showed such a decrease. In a study of 308 cases of peptic ulcer it was found that aluminium hydroxide was a much more effective neutralizer over a long-term period than Sippy powders.

E. N. Collins, C. P. Pritchett, and H. R. Rossmiller followed up 246 cases of peptic ulcer treated with aluminium hydroxide. The largest number of patients (154) were examples of uncomplicated duodenal ulcer, and of these 97.4 per cent gave satisfactory results. Of 51 patients with massive haemorrhage from duodenal ulcer, 80 per cent were satisfactory. Of 21 patients with pyloric obstruction, 19 obtained relief, and of 12 of these cases which were followed up, good results were maintained in all. Of 37 cases of gastric ulcer, good results were obtained in 33, or 89 per cent. Of 8 cases of multiple ulcers, 6 did well. Five of 7 patients with marginal or anastomotic ulcers made satisfactory progress.

J. B. Kirsner, from investigation of the effect of aluminium hydroxide on the acid-base balance and on renal function in 23 patients with peptic ulcer, concludes that even in massive doses given over long periods of time, the drug did not cause any decrease in renal efficiency, and it can be given with complete safety to patients with a marked reduction in renal efficiency. It does not disturb the acid-base balance.

Colloidal aluminium hydroxide.—E. E. Woldman reports on 144 cases of massive haemorrhage from gastric or duodenal ulcer treated by the continuous administration of colloidal aluminium hydroxide. The mortality rate in this series was 2 per cent as contrasted with a mortality rate of 28 per cent before this treatment was employed. The advantages of the method are as follows. It is a harmless non-absorbable astringent which is capable of hastening the formation of a clot; being antacid it can prevent the digestion of the clot by continuous neutralization of the excess acid in the stomach, without danger of causing alkalosis; forming a gelatinous mass it acts as a mechanical protection to the lesion. Thus it arrests the bleeding, protects the ulcer, and facilitates healing. The aluminium hydroxide diluted to a 33½ per cent suspension is continuously instilled into the stomach through a naso-gastric tube at the rate of about 15 drops a minute, day and night, for 10 days.

Syntrogl.—F. Spindler reports on the use of syntrogl, a preparation containing aluminium hydroxide, 3-diethylamino-2:2-dimethyl-1-propanol-*dl*-tropicacidester, bismuth subcarbonate, calcium carbonate, and oil of peppermint, in the treatment of hyperacidity and peptic ulcer. Cases comprised those of duodenal ulcers and those of simple hyperacidity. In all cases some degree of relief of symptoms was obtained, but it is doubtful if this relief was greater than that obtained by the use of aluminium hydroxide alone.

Aluminium phosphate gel.—G. B. Fauley, S. Freeman, A. C. Ivy, A. J. Atkinson, and H. S. Wigodsky present a report showing that large doses of aluminium hydroxide gel interfere with absorption of phosphates in man, and may produce a phosphorus deficiency in the presence of a relative deficiency of pancreatic juice, of diarrhoea, or of a low-phosphorus diet, although it should not produce a deficiency in the usual patient on the ordinary ulcer diet. It

had previously been shown experimentally that aluminium hydroxide gel did not prevent the occurrence of post-operative jejunal ulcer. The authors investigated the therapeutic properties of aluminium phosphate gel experimentally for the healing of jejunal ulcers produced in dogs by the Mann-Williamson operation, namely: gastro-jejunostomy, and diversion of the pancreatic juice and bile into the terminal part of the ileum. After ulceration appeared, as a result of cessation of the preparation, re-administration of aluminium phosphate gel caused complete healing in 9 out of 10 dogs. The results of the use of aluminium phosphate gel in patients with peptic ulcer (duodenal 32, gastric 2) and 3 patients with jejunal ulcer indicates that aluminium phosphate gel appears to be as effective as any other preparation employed in the treatment of peptic ulcer.

Magnesium trisilicate.—M. Kraemer states that magnesium trisilicate approaches the ideal antacid. It has a prolonged neutralizing effect *in vivo*, is tasteless, non-astringent, is neither constipating nor laxative, is insoluble, has a prolonged action, and does not stimulate a secondary acid rise. It cannot cause alkalosis, and does not give rise to the formation of gases.

Meulengracht régime.—J. Chasnoff, S. Leibowitz, and R. Schwartz report the results obtained in 21 cases of bleeding peptic ulcer treated with the Meulengracht régime, and compares them with a control group of 72 cases treated with the older 'starvation-Sippy' method. The mortality rate in the Meulengracht series was 4.76 per cent, a decided improvement over the 11.1 per cent in the control group. The patients receiving early liberal feeds showed a well-being not noted in those under the older method of treatment. Two of the 21 cases were further complicated by the occurrence of perforation; this occurred in only 1 patient in the control series.

Bleeding ulcers.—Suggestions for the treatment of bleeding peptic ulcers are made by I. J. Wood, who lays stress on preliminary observations on the history of bleeding, blood pressure, pulse rate, and haemoglobin percentage. The last falls immediately during blood loss, while the pulse rate and blood pressure may still be normal. Rest is essential to the patient and persistent disturbing procedures should be avoided. The diet should contain plenty of water, abundant carbohydrates, moderate protein, salt, and an ample supply of vitamins B and C. Small doses (15 grains daily) of ferrous sulphate may be given to patients who have lost much blood. Massive blood transfusions are recommended if the haemoglobin count falls below 40 per cent or the systolic blood pressure below 90 millimetres of mercury; if the patient has collapsed; or before ligation of a bleeding vessel. Its efficacy cannot be judged solely by the survival or death of the patient, as death is often the result of secondary effects due to prolonged haemorrhage. Surgical intervention should be avoided until at least one attempt to restore the haemoglobin level has failed, but should be employed before the fifth attempt. The main surgical problems are the location of the ulcer; the relative merits of resection and radical gastrectomy, and the justification for a blind partial gastrectomy which may include one of the common sites of fatal haemorrhage. Repeated haemorrhage impairs the recuperative power of the stomach wall.

Treatment of complications.—S. C. Franco reviews 130 cases of peptic ulcer; the youngest patient was 18 and the oldest 82 years of age. The basis of treatment was immediate and repeated feeding, and the routine use of transfusion and parenteral fluids. Franco reports the following incidence of complications. Haemorrhage occurred in 31 cases. There were 17 cases of acute perforation, 12 from gastric ulcer, 4 from duodenal ulcer, and 1 from marginal ulcer. The treatment was operation and simple closure of the perforation. There were 10 cases of chronic perforation. Pyloric stenosis occurred in 17 cases, and in these the general condition of the patients was improved and the stomach allowed to diminish in size before operation. The author believes that gastric ulcers do not induce malignant changes, but that these malignant lesions begin as such.

Gastro-Jejunal Ulcer

Clinical picture and morbid anatomy

M. M. Montgomery and J. D. Kirshbaum review the subject of gastro-jejunal ulcer in full detail and add an account of 8 cases with necropsies seen at the Cook County Hospital among 13,000 consecutive necropsies from 1929 to 1940. The ulcers are practically always associated with gastro-jejunostomy with or without gastric resection. They may be confined to the jejunum, usually within 2 centimetres of the stoma, or involve the margin of the stoma of the gastric mucosa (gastro-jejunal or marginal ulcer). Von Eiselsberg (1914), Judd (1921), and Moynihan (1923) estimated their incidence at 1 or 2 per cent of the original operations. Balfour reported that jejunal ulcer was twenty times more frequent after operations for duodenal ulcers than after those for gastric ulcers. According to Hurst and Stewart the ulcers may follow any form of partial gastrectomy. All the eight cases, of which one patient had two ulcers, detailed by the authors were in white males, with an average age of 49 years, the youngest being 40 and the oldest 60. The interval between the original operation and the onset of jejunal ulcer varied from 6 weeks to 21 years, the average being 11.4 years. The interval between the recurrence of symptoms and the fatal complication was usually, except in 2 cases, a few weeks. The cause of death was perforation with peritonitis in 3 cases, fatal haemorrhage in 2 cases, perforation followed by abscess in 1 case, intestinal obstruction in 1 case, and barbiturate poisoning in 1 case. The original operations included 6 posterior gastro-enterostomies, 1 gastric resection, and 1 exclusion operation in which the distal half of the stomach was made continuous with the duodenum and the proximal half was anastomosed

to the jejunum. The cause of the ulcer is still obscure and will be until the problem of peptic ulcer in general is solved, and is probably the same in both cases. The vulnerability of the jejunal mucosa to the acid gastric juice is important. Other hypotheses mentioned are von Bergman's idea of vascular spasm, Konjetzney's suggestion of local infection, and the constitutional conception. The ulcer may be acute, subacute, or chronic, and microscopically may resemble a peptic ulcer.

Complications

Gastro-colic and gastro-jejuno-colic fistula.—In the commentaries and radiograms of his report on 5 cases of gastro-colic and gastro-jejuno-colic fistula, E. R. Williams deals with the diagnosis especially by radiological methods. Gastro-colic fistula is usually the result of a gastro-jejunal ulcer secondary to gastro-jejunostomy, but it may be due to a primary carcinoma of the colon or stomach invading and perforating into the adjacent viscus. A most exceptional event is perforation into the stomach from the colon as the result of ulcerative colitis; this occurred in one of his cases, the patient being a woman, aged 38, with a history of moderately severe ulcerative colitis for 10 years; a barium enema showed a fistulous track leading from the splenic flexure into the stomach, which eventually filled considerably; a consequent operation showed that there was not any evidence of carcinoma. The clinical features of gastro-colic fistula are: foul eructations and faecal vomiting; lenteric diarrhoea immediately after a meal, the stools containing much undigested food; loss of weight; and a change in the characters of the pain in gastro-enterostomy cases. In routine barium work, both meal and enema, a gastro-colic fistula may be missed. The only indirect sign of any value as a clue is the early appearance of barium in the transverse or descending colon before the caecum shows any trace of barium. In cases of intestinal haste a barium enema should be given; in cases of intestinal haste with a fistula the sigmoid and rectum may, soon after a barium meal, be loaded with barium without there being any in the caecum.

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PERITONEUM: NON-INFLAMMATORY DISEASES

See also B.E.M.P., Vol. IX, p. 528.

Tumours

Primary

Malignant.—J. H. Levy and E. R. Pund report 2 cases of primary sarcoma of the omentum, a rare condition, difficult to diagnose before operation, and with a high mortality. In both these cases, as in a considerable proportion of the 84 previously published examples, the growth apparently arose from the vascular endothelium. The onset is generally insidious, with bizarre abdominal symptoms. There is as a rule vague abdominal discomfort with a dragging sensation. The onset is occasionally acute with severe abdominal pain. Torsion of the omentum may also produce an acute abdominal crisis with surgical shock. General malaise, anorexia, loss of weight, nausea, vomiting, constipation, and sometimes diarrhoea are the most frequent initial symptoms. Abdominal distension due to ascites is present in more than half of the cases. Pressure symptoms and partial intestinal obstruction may occur. The abdominal tumour is usually in the middle line, and in some instances it is mobile and can be pushed from side to side and upwards, though not, generally, downward. This serves

to distinguish it from a primary pelvic growth. The mass is not as a rule tender. It is not generally influenced by respiration.

Hydrocele of Canal of Nuck

Differential diagnosis

V. S. Counsellor and B. M. Black report 13 cases of hydrocele of the canal of Nuck. Diagnosis of the condition is difficult; the most important differential diagnostic procedure to distinguish hernia from hydrocele is transillumination. The wall of the hydrocele consists chiefly of fibrous tissue with a single layer of flattened cells on the inner surface. Smooth muscle may be present in the wall.

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PERITONITIS: ACUTE PERITONITIS

See also B.E.M.P., Vol. IX, p. 537; Cumulative Supplement, Key No. 1241; Surveys and Abstracts 1940, p. 443; and p. 13 of this volume.

Treatment

Alcohol lavage

R. J. Behan, A. B. Sigmann, W. Ruehl, and J. A. Zewe recommend, in cases of suppurative generalized peritonitis, lavage of the abdominal cavity at the time of operation with 70 per cent alcohol. When the abdomen is opened 100 to 200 cubic centimetres, or more, of alcohol are introduced, allowed to remain for a few minutes, then siphoned off by a suction apparatus. If the contents of the abdominal cavity are particularly foul and there is a large quantity of sero-fibrinous exudate, alcohol is poured in and siphoned off alternately until the return flow is clear. The authors found that, with this method, the temperature falls to normal in about 9 days as compared with 12·5 days when alcohol is not used. The time spent in hospital is reduced (5·5 days). The death rate in a series of cases of generalized peritonitis thus treated was 8·69 as compared with 45·39 per cent in cases not treated with alcohol.

Behan, R. J., Sigmann, A. B., Ruehl, W., and Zewe, J. A. (1940) *Amer. J. Surg.*, **50**, 92.

PERITONITIS: CHRONIC PERITONITIS

See also B.E.M.P., Vol. IX, p. 547.

Adhesive Peritonitis

Paraffinoma as a result of liquid paraffin treatment

A. H. Cruickshank reports a case of a man, aged 45, with intestinal obstruction due to adhesions. At operation half a pint of liquid paraffin was left in the peritoneal cavity with the object of preventing further adhesions. Three years later intestinal obstruction recurred and at the laparotomy the intestines were densely matted together by adhesions, and multiple paraffinomas were found on the peritoneum and mesentery and some free in the peritoneal cavity.

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PHARMACOLOGY

See also Surveys and Abstracts 1939, p. 471; 1940, pp. 127 and 444; and p. 111 of this volume.

Acriflavine Components

Bacteriostatic values

Acriflavine and proflavine.—H. Berry reports his observations on the components of acriflavine which consists of a mixture of the hydrochloride of 2:8-diamino-10-acridine and of 2:8-diamino-10-methylacridinium chloride containing approximately one-third of its weight of the dihydrochloride. He found that mixtures containing 30 per cent of 2:8-diaminoacridine are only slightly more soluble than the pure components or other mixtures. The solubility of the components and mixtures is less than that of commercial acriflavine. No definite eutectic or compound is formed. Mixtures do not possess greater bacteriostatic power than either of the components. Against streptococci the methylchloride is more active than the diaminoacridine. The bacteriostatic values obtained resemble those recorded for acriflavine. It is suggested that on account of these results, together with the greater toxicity of acriflavine, proflavine should be used in preference to acriflavine. The solubility of proflavine is about 1 in 300, but is sufficient for the preparation of the solutions used in practice. The best derivative for use is the neutral hydrochloride of the 2:8-diaminoacridine.

Effect in the prevention of nasal sepsis and post-operative scarlet fever

Acriflavine and proflavine.—G. Young and A. A. Charteris report on the value of proflavine and acriflavine in the prevention of sepsis during radium therapy of malignant tumours of the accessory nasal sinuses, and in the prevention of post-operative scarlet fever. Radium applicators placed in the accessory sinuses are held in position with packing soaked in proflavine oleate, 1 per cent in liquid paraffin. This procedure has been found by the authors to prevent the gross sepsis which was so apt to occur before the use of this packing. No local or other complications have been found to follow treatment, even when the operative field has been extensive. All patients entering the throat and nose wards have for 6 years been given a mouth-wash and gargle of an aqueous solution of acriflavine, 1 in 5,000, twice daily.

Before the introduction of this method, one of the wards had been closed 13 times in one winter for scarlet fever, but during the 6 years of its employment, only 5 cases of post-operative scarlet fever have occurred.

Action of Various Drugs on the Nasal Mucosa

Antiseptic snuffs

M. E. Delafield, Edith Straker, and W. W. C. Topley report the results of an investigation of the effects of three antiseptic snuffs—of proflavine, penicillin, and sulphathiazole respectively—on the bacterial flora of the nose, the nasopharynx, and the tonsillar region. As a preliminary a number of substances, including ordinary tobacco snuffs and lycopodium snuffs containing sodium sulphate with or without menthol, were tested to see if stimulation of the normal nasal discharge exerts any bactericidal effect. The results were not promising, and attention was then turned to the other three snuffs mentioned above. After 9 subjects had received proflavine, and also other forms of snuffs, the use of proflavine snuff was given up. The following cautious conclusions are reached from the examination of the investigations of 20 subjects: an antiseptic snuff containing sulphathiazole or penicillin may lessen the incidence of effective invasion of the nose by bacteria or the invasion of the nasopharynx through the nose. It may therefore be of use as a prophylactic against bacterial infections of the upper respiratory tract; but there is not any evidence that it will prevent or cure the common infective cold, although it may favourably affect the course of a cold by the prevention of secondary bacterial infection; it may perhaps cure nasal carriers of staphylococci or reduce the number of vegetative organisms, and in view of its action on diphtheroids, it is desirable to test its possible use in the treatment of nasal carriers of diphtheria bacilli. As none of the antiseptic snuffs tested have had any effect on the nasopharyngeal or tonsillar flora an attempt was made to bring this about by the use of tablets containing proflavine, but without positive results. A trial has been started of oral insufflation of antiseptic powders.

Action of Various Drugs on Skin

Pre-operative treatment

J. M. Clarke outlines the essential properties of pre-operative skin preparation, namely sterility, low cost, simplicity in application, well-outlined field, harmlessness to patient, linen, and instruments. The New Zealand hospitals' routine is given as: shaving and cleansing with ether soap; washing in sterile water; removal of fats by sulphate of ether; application of 1:1,000 biniodide of mercury in spirits; covering with sterile towel; painting with iodine. The whole preparation is repeated 2 or 3 times. It is criticized on the grounds of cost, irritating effect of mercurial salts and iodine, poor outline, and the doubtful action of mercuric biniodide. Recent reports are reviewed and the conclusion is reached that there is great divergence of opinion on different preparations. Mercurial solutions are favoured by some but not by the author, and by Price who recommends caution in its use. Iodine condemned by Bonney and Browning is recommended by Meleney. Sixty per cent alcohol claimed to be worthless by Price is used with effect by the author, who suggests that differences in sterility tests and application to different parts of the body may account for the disagreements. He carried out bacteriological tests on 20 unselected abdominal patients, using the following preparation: shaving and cleansing with hand soap; drying; liberal application of 60 per cent methylated spirit tinted with aniline red; sterile covering; the preparation being made on the day before and on the day of the operation. In all cases sterility was obtained after two preparations but not often after one. Clinical results confirmed the sterility.

Amino-Acetic Acid and Gelatin

Effect on muscular fatigue

G. L. Maison, following up the observation of G. B. Ray, J. R. Johnson, and M. M. Taylor that gelatin was an effective agent in postponing human fatigue, investigated this point in 2 males in order to test the work ability of a single human muscle before, during, and after the ingestion of gelatin or amino-acetic acid. Neither amino-acetic acid, in doses of 15 grammes daily for 30 days, nor gelatin, in doses of 60 grammes daily for 40 days, was found to increase the work ability of the extensor digitorum communis muscles working with or without blood supply. In 4 subjects in the midst of a training period the ingestion of gelatin for from 20 to 30 days did not produce any obvious difference between the rate of training of those taking gelatin and the rate of training of controls without gelatin.

Aminophylline

Effect on peripheral blood flow

H. J. Stewart and N. B. Jack utilized the average skin temperature for the measurement of the peripheral blood flow and changes in this resulting from the intravenous injection of aminophylline. In 21 out of 25 cases, the injection of 0.48 gramme of the drug increased the flow, but for a few minutes only. Rapid injection of the drug intensified this effect. The increase was accompanied by a fall in skin temperature caused by sweating, and as the skin became cooler the body lost more heat. The skin temperatures of the hands and feet varied much more than those of other parts of the body. Aminophylline did not produce any significant changes in oxygen consumption. In the above dosage the drug increases the cardiac output, and the increased amount of blood is available for the augmented circulation in the skin, without redistribution of the circulatory blood volume.

Ammoniated Mercury Ointment*Idiosyncrasy in children*

M. H. Bass reports 5 cases of idiosyncrasy to ammoniated mercury ointment in children. In spite of the serious clinical picture of high fever, prostration, extreme oedema, and generalized erythema, the prognosis is excellent, and recovery without any serious sequel is the rule. Individuals showing idiosyncrasy are sensitive to very small amounts of the drug.

Arsenical Compounds*Effect on trypanosomes*

Tryparsamide.—F. Hawking reports on the trypanocidal activity and arsenic content of blood serum after the injection of tryparsamide. Immediately after the intravenous injection of the drug, the trypanocidal activity of the serum against trypanosomes of a serum-resistant strain of *T. gambiense* was absent; it rose to a maximum at 24 hours, then gradually diminished until, 4 days after injection, it was inappreciable. The drug disappears from the blood very rapidly after injection; in 2 persons the arsenic content of the plasma, 24 hours after injection, was only 0.07% of arsenic per millilitre.

Harmful effects

Arsphenamine encephalopathy.—N. A. Levy reports a case of arsphenamine encephalopathy, in a male aged 19, in whom the unusual features were a severe meningeal inflammatory reaction, and an intense leucocytic and lymphocytic infiltration of the vessel walls and parenchyma of the brain, in addition to the usual vascular necroses and perivascular haemorrhages.

Jaundice.—F. M. Hanger, Jun. and A. B. Gutman report 12 cases of post-arsphenamine jaundice which appeared to be due to obstruction of the intrahepatic biliary tract. This appears to be a distinct form of reaction to intravenous arsenicals characterized by acute onset with constitutional and gastro-intestinal symptoms appearing several hours after the second or third injection; the appearance within several days of jaundice which may persist for weeks or months; laboratory evidence of obstructive jaundice with little or no sign of liver-cell degeneration; essentially normal liver cells in liver biopsies; and eventual recovery of the patient.

Acute interstitial myocarditis.—C. E. Brown and D. H. McNamara report a case of acute interstitial myocarditis complicating exfoliative dermatitis resulting from arsphenamine therapy. This occurred in a man 34 years of age, who had received 6 bi-weekly injections of 0.6 gramme of arsphenamine, with complete disappearance of the cutaneous lesions and throat symptoms at the end of the second week. Five weeks later he received 0.6 gramme of neoarsphenamine; 2 days later a generalized dermatitis developed, which became so severe that he was admitted to hospital. Several days later he died from myocardial failure. The authors suggest the probability of an allergic aetiology for the myocarditis.

Mapharside

After recovery from arsphenamine dermatitis.—A. G. Schoch, L. J. Alexander, and W. E. Long state that mapharside can generally be successfully administered to patients after recovery from arsphenamine dermatitis, provided that the dermatitis is less severe than that of exudative exfoliative dermatitis requiring treatment in hospital. The initial dose recommended is 1 milligram, and not more than 5 milligrams. The authors employed the drug in 40 such cases; 30 of these patients tolerated mapharside in full therapeutic doses, but the other 10 showed cutaneous intolerance to the drug in doses of 5 milligrams or less.

 β -Erythroidine Hydrochloride*In encephalitis epidemica*

V. W. Eisenstein and M. Tarlau report on a clinical trial of β -erythroidine hydrochloride in 8 patients with chronic encephalitis with parkinsonism and in 3 cases of infantile cerebral palsies (Little's disease). All were adults in whom the disease had been established for 10 years or longer. The youngest patient was 32, and the oldest 59. A 10 per cent solution of β -erythroidine hydrochloride dissolved in distilled water was employed, sterilized by filtration. It is concluded that the drug, which possesses a curare-like pharmacological action, has a slight inconstant transient loosening action on skeletal musculature in hypertonic states. These effects are, however, accompanied by such constant and undesirable side-effects as to contra-indicate the clinical use of the drug. The drug has not any effect on tremor.

Barberry Root*Antiseptic properties*

G. F. Dick investigated the antiseptic properties of an infusion of algerita root (*Berberis trifoliatis* Moric). Five hundred grammes of the crushed root were boiled for 30 minutes in 2 litres of distilled water, and the liquid filtered through gauze. This was tested against various organisms, and it was found that haemolytic streptococci and diphtheria bacilli were killed in one-fifth the amount of infusion required to kill staphylococci and pneumococci. The author concludes that the berberine content of the infusion had the antiseptic effect.

Barbiturates*As sedatives*

Clinical uses.—H. P. Hampton and F. P. Moersch point out that of the most often prescribed and abused drugs affecting the autonomic functions, cathartics are now given more wisely, but that medical practitioners are still liable to censure for the use of sedatives. Discussion

of the popular drugs employed in sedation now is largely confined to the barbiturates, which are, however, often regarded as more innocent than they really are, especially in some persons who crave for them. There is also a demonstrable shortening of the duration of effect after periodic ingestion. Addition to large doses may cause accumulation of depressive effects and irreparable damage to the brain. There is a growing clinical impression that in organic disease of the brain, such as sclerosis and tumour, the barbiturates often do harm. They are strikingly alike except for the duration of effect, which is short except in phenobarbital and barbital. The sedative derivatives of barbituric acid are useful in the treatment of situational insomnia, in pre-anaesthetic medication, and in depressing motor activity. Some of the older sedatives, such as chloral hydrate, the bromides, and paraldehyde, have fallen into undeserved neglect. Chloral hydrate is one of the most reliable of sedatives, especially in agitated and convulsive states; it cannot be given hypodermically, addiction is not common, it produces drowsiness in 15 minutes and sound sleep in 1 hour. The blood pressure is slightly lowered and the pulse slowed, but there is not any good evidence that it depresses the heart. Paraldehyde has an action similar to that of alcohol, but has a more powerful hypnotic effect. Bromides are much in disrepute at present, but should not be discarded; they produce mental calm but do not enforce sleep.

Benzyl- β -dimethylamino- α -phenyl- α -ethylpropionate hydrochloride

Anti-spasmodic action

Compared with papaverine.—K. Unna reports on the pharmacological action of benzyl- β -dimethylamino- α -phenyl- α -ethylpropionate hydrochloride, a new synthetic substance. The antispasmodic action of this drug was demonstrated on isolated organs and on the intestine *in situ*. Its mode of action is similar to that of papaverine in that it acts directly on the smooth muscle fibres. When tested on isolated organs, the benzyl ester is more effective than papaverine in equal concentrations. In contrast to atropine the benzyl ester has little or no effect on the parasympathetic nervous system. Intravenous injections of the benzyl ester produce a transient drop in blood pressure due to vasodilatation. The vasodilator effect, as demonstrated in perfusion experiments on frogs and by leg plethysmography in cats, is comparable to that of papaverine. The oral, subcutaneous, and intravenous toxicity of the benzyl ester, as studied in mice or rabbits, is lower than that of papaverine.

Bromides

Bromide intoxication

Dosage.—In a paper on bromide treatment and intoxication F. Pilkington points out that it is not generally recognized that there are considerable variations in the dosage necessary to bring out the best therapeutic effects, and that when this has been found the drug should usually be given for several weeks. The occurrence of bromide intoxication is discussed; two cases, in one of which the patient was almost moribund at the peak of the intoxication, are related in detail. The treatment advocated consists of large quantities of bland fluids, 30 grains of sodium chloride every 4 hours, and bromides absolutely stopped. Pilkington states that levels of under 100 milligrams of bromide per 100 cubic centimetres of blood may generally be considered safe during bromide therapy. The greater the consumption of salt, the more rapid is the excretion of bromide. A useful initial dose of bromide is 10 grains 3 times a day, but double this dosage may be given. Watch should be kept for the occurrence of symptoms of bromide intoxication. It is the exception rather than the rule to see an acneiform eruption.

Chlorophyll

Antiseptic action

B. Gruskin advocates the use of chlorophyll in the treatment of acute or chronic local suppurative conditions. The chlorophyll employed by the author was in the form of the water-soluble derivatives of chlorophyll, sodium magnesium chlorophyllin, sodium iron chlorophyllin, sodium copper chlorophyllin, the oil-soluble chlorophyll A and chlorophyll B. Chlorophyll is indicated in the treatment of open wounds and of deep infections associated with drainage tracts communicating within the body cavities of the abdomen and chest. For open wounds dressings soaked in chlorophyll solution may be applied as often as necessary without fear of irritation of the skin. Packs saturated with the solution are of value in the treatment of acute rhinitis and rhino-sinusitis. Ointments containing oil-soluble chlorophyll are useful in the treatment of chronic ulcers, especially those of the indolent varicose type, and in impetigo contagiosa. The ointment consists of 1 gramme of chlorophyll in 28 grammes of lanolin. The author suggests that chlorophyll acts by increasing the resistance of the cell membrane so that enzymic digestion by invading bacteria or their toxins is checked.

Choline Derivatives

In asthma

Parasympathetic tropism of acetyl- β -methylcholine.—H. H. Moll observed the effect of parasympathetic-mimetic drugs in cases of asthma and of other chronic respiratory diseases. Acetyl- β -methylcholine was used owing to its tropism for the bronchial nervous system. Asthmatic subjects almost invariably responded with respiratory symptoms varying from slight wheeziness to a severe asthma-like attack. Control subjects showed general signs of parasympathetic stimulation, but chest symptoms did not follow. The parasympathetic tropism of choline derivatives in bronchial asthma appears to be due to a local increased sensitivity of the bronchial nerve endings or of the bronchial muscle. Lung damage is essential in the

occurrence of the abnormal bronchial response. The test with this drug should assist in the differential diagnosis between true bronchial asthma and hysterical hyperpnoea. No matter how mild or infrequent the attacks of asthma may be, an asthmatic subject is nearly always susceptible to the drug.

Effect on the heart

Acetylcholine.—A. E. Cohn and A. G. Macleod show that by a simultaneous record of intracardiac pressure, pulses and electrograms, the effect of acetylcholine on the cardiac auricles is to reduce the force of contraction and the duration of the excited state, and frequently to produce fibrillation. Acetylcholine has a similar, but much slighter, effect on the ventricles.

Colchicine

Effects after partial hepatectomy

C. H. Scheffley and G. M. Higgins report the results of their experiments on the effect of colchicine after partial removal of the liver. In 40 male white rats 70 per cent of the liver was excised and a saline solution of colchicine injected hypodermically into the rats on successive post-operative days; all the rats given colchicine on the first 3 post-operative days died within 48 hours; there were not any deaths among the rats injected after the fifth post-operative day. Little regeneration of liver tissue occurs during the first 2 days after partial hepatectomy. A series of rats that had undergone removal of one kidney served as controls; when colchicine was given deaths did not occur on the first or other post-operative days. It was therefore possible to estimate the toxicity of a drug in relation to the amount of hepatic tissue present, since in this investigation the toxic effects of colchicine were, as measured by mortality, inversely proportional to the amount of liver present. The harmful effects of many toxic agents are increased in patients or animals with hepatic disease. The evidence presented does not justify the conclusion that colchicine is detoxified by the liver, but it does suggest that the drug should be cautiously used in patients with hepatic disease.

Coramine

Effect on abnormal respiratory rate

In heart disease.—W. D. Stroud and P. H. Twaddle state that coramine (nikethamide) may exert a beneficial effect on the abnormal respirations associated with cardiac disease. Oral administration does not generally give rise to dramatic results, but rather a slow progressive improvement; as a rule one to three days elapse before the maximal benefit is obtained. A more prompt but transient response results from intravenous administration of the drug, and 5 cubic centimetre doses may cause symptoms of wide-spread cerebral stimulation. The prolonged use of coramine does not always improve cardiac efficiency. A decline in intrathecal pressure, and to a less constant and striking degree, in venous pressure, results from intravenous injection. The authors doubt if these pressure changes are directly related to the improvement noted. Coramine appears to stimulate the respiratory receptors, either peripherally or centrally.

Digilanid

Effect on heart

R. C. Batterman, D. V. Holman, and A. C. De Graff report on the therapeutic efficiency and the potency of digilanid, a mixture of pure crystalline glycosides present in *Digitalis lanata*, in 23 hospital patients and 20 ambulatory patients with heart disease. They found that the drug is readily absorbed and that its efficacy appeared to be identical with that of powdered digitalis leaf. In terms of cat unit potency, the therapeutic and toxic doses of the drug were identical with those of *Digitalis purpurea*. There were not any symptoms of gastro-intestinal irritation among the 43 cases. The authors conclude that the drug satisfies to a high degree the criteria for a satisfactory digitalis preparation.

Drugs for Nose

Contra-indications

F. J. Novak, Jun. states that the use of any medicament in the nose, except ephedrine in physiological saline solution, is hazardous for some persons. No type of oil should be used in the nose of persons with lesions of the tongue or pharynx, or with hemiplegia or other neurogenic disturbance. The same applies to practically all the commonly employed drugs, whether in oily or aqueous vehicles. Infants, debilitated children, and the aged are more likely to aspirate fluids taken into the nose or orally, and for such people the use of liquid paraffin or any other kind of oil is clearly contra-indicated. If oil is used, vegetable oil is preferable to mineral oil.

Face Powder

Removal

Water-soluble base.—R. G. Harry finds that powders, if applied over a vanishing cream or other water-soluble base, are readily removed from the skin by ordinary washing in soap and water. They can also be removed if applied directly to the skin, but not quite so readily as when applied over a vanishing cream. They are removed only with difficulty under ordinary face-washing conditions if applied on top of a cold cream or water-in-oil base. Cleansing milks appear to possess superior detergent powers for coloured make-up and for certain types of skin dirt, but in such cases they should be removed from the skin by frequent rinsing.

by water. In the local treatment of greasy skins it would appear best either to avoid powders, or to remove excess sebum by means of a suitable degreasing agent.

Helium-Oxygen Mixtures

Effect on voice.—W. B. Dublin, E. J. Baldes, and M. M. D. Williams state that efficient administration by inhalation of a mixture of helium and oxygen is accompanied by a change in voice, consisting in a variation in overtones. The frequency of the fundamental vibrations remains the same. Because of the relatively low density of helium compared with that of nitrogen, a mixture of helium and oxygen may impede the vibration of the vocal cords less than air. This may result in a change in the original production of overtones. Also, because of lower density, the velocity of sound is increased in helium-oxygen mixture. This probably causes the vocal resonators to amplify different overtones.

Heparin

Prevention of blood clotting

Use in surgery and thrombosis.—G. Murray successfully employed heparin to prevent clotting in arterial suture, arteriovenous fistula, venous grafts, embolectomy, mesenteric thrombosis, thrombophlebitis, phlebothrombosis, and pulmonary embolism. In a series of 700 cases toxic effects were not observed. There are not any contra-indications to the use of heparin, except in the case of a patient who has active bleeding from an open vessel, in which event the prolonged clotting time would encourage the bleeding to continue.

Use in prevention of post-operative thrombosis

C. Crafoord and E. Jorpes demonstrate the use of heparin as a prophylactic against post-operative thrombosis. Three hundred and twenty-five patients were treated. The usual dose was 50 + 50 + 50 + 100 (or 75 + 75 + 75 + 125) milligrams daily given intravenously as a 5 per cent sterile solution over a period of 5 to 10 days. The concentration was 70 per cent that of the pure mucoitin trisulphuric ester. There were no thrombo-embolic symptoms, whereas in a control group of 1,111 untreated patients, 9 per cent of them had post-operative complications. The treated patients were all over 35 years of age and had had operations performed on the gastro-intestinal tract, the biliary system or urinary passages, or major operations for hernia and varices. Heparin was also given to 88 patients operated on for myoma or prolapsus uteri. There were no complications, whereas in a control group of 1,054 patients 4 per cent of the patients had post-operative complications.

Hormones

Desoxycorticosterone acetate

Effect on endometrium.—E. C. Hamblen, W. K. Cuyler, C. J. Pattee, and G. J. Axelson studied the metabolism of, and the endometriotropic responses to, injected desoxycorticosterone acetate in 8 women. There were not any significant changes in the urinary excretion of 17-ketosteroids, determined by Oesting's method, or of sodium pregnanediol glucuronide, determined by Venning's method. In spite of priming the endometria with oestrogens before treatment, progestational changes were not produced in the endometria of the 5 patients investigated.

Effect on embryo implantation.—H. O. Burdick and E. J. Konanz found that the daily injection of 2 milligrams of desoxycorticosterone acetate, begun on the day of mating of albino mice, prevented embryo implantation. If the first injection was delayed until the day following mating (approximately 40 hours after ovulation) embryos were implanted, and increased luteinization and vascularity were in evidence throughout the period of observation. This appears to support the belief that the adrenal cortex is an important factor in the performance of the ovary.

Oestradiol and desoxycorticosterone acetate

For normal infants.—R. A. Miller studied the effect of oestradiol and desoxycorticosterone acetate therapy in normal infants during the first 10 days of life. Twenty infants were given 1 milligram of oestradiol dipropionate intramuscularly on the first day of life, and this was repeated on the fourth day in 10 of the cases. Another group of 20 infants was given desoxycorticosterone acetate, 5 milligrams by intramuscular injection on the first, fourth, and tenth days. A further group of 20 infants was employed as a control. There were not any toxic symptoms. The weight progress of female infants appeared to be aided by oestradiol and the maximal physiological loss of weight at birth diminished. The gastric acidity was not influenced by the hormone therapy.

Oestrogens

New derivatives.—In his Cameron prize lecture at Edinburgh, E. C. Dodds begins with a review of the history of therapeutics, as modern developments have obscured the early application of chemistry to the treatment of disease. This carries the history of endocrinology up to the clear-cut example of the thyroid, and the main subject of the lecture, 'The New Oestrogens', which follows is not such a complete picture. The early work was based on the assumption that the secretions of the endocrine glands were specific in action, and that this action could not be imitated by any other agent; there was little interest in the question of finding synthetic substitutes for the female sex hormone. After Aschheim and B. Zondek's discovery of the hormone excreted in the urine of pregnant animals it was possible to crystallize out substances, and here a tribute is paid to Marrian for his isolation of the crystalline substance oestriol. Oestrone, the first to be thus isolated in crystalline form, was for some

time regarded as the true ovarian hormone, but when oestradiol was first obtained by a process of partial hydrogenation and found to be about five times as active as oestrone, it was considered to be the true hormone of the ovary, a view strengthened when it was isolated from the follicular fluid. Other oestrus-producing compounds were equilenin and equilene, which, being less active and not easily obtained, are not of clinical importance. Oestrone and especially oestradiol are the only naturally occurring oestrogenic substances in clinical use. But the fact that there are as many as five different oestrogens led to the investigations which produced the synthetic oestrogenic analogues. The large number of compounds concerned suggested that the oestrus reaction did not demand the specificity that has always been associated with complex biological reactions, or alternatively that these reactions were as a class not nearly so specific as had been believed. A whole series of synthetic substances with oestrogenic activity has thus been made available, especially stilboestrol; these, in contrast to the expensive naturally occurring hormones, are within the reach of a wide circle of patients. It would appear from published reports that the immediate practical value is now assured, but they are plainly of wider importance. It is not perhaps too much to hope that just as aspirin marked the beginning of a new era in medicine, so these compounds may be the first steps on the road to great advances in the treatment of disease. There is little doubt that similar analogues can be made for other sex hormones and for adrenal cortical hormone, and possibly similar advances may be made in connexion with the vitamins. There is every indication that the part played by chemistry will make the years to come as fruitful in the fight against disease as the last hundred years have been.

Pitressin

Effects in cardiovascular disease.—A. Graybiel and R. E. Glendy report the effects of intravenous injection of a dilute solution of pitressin, 1 in 1,000 of saline, for 30 minutes to 1 hour or more to 9 normal persons, 4 patients with essential hypertension, and 2 patients with coronary disease. Significant cardiovascular symptoms were not observed in the normal persons or in those with coronary disease. Almost immediately, however, there was pallor of the skin and mucosa, pointing to marked constriction of the minute vessels and of the large arteries, but not of the arterioles. Abdominal symptoms occurred in all cases in the form of nausea, epigastric discomfort, cramp-like borborygmi in the lower abdomen, and sometimes evacuation of the lower bowel. Pitressin thus given has a cumulative effect, the limiting effect being gastro-intestinal. Angina was not reproduced in two patients with coronary disease who received sufficient pitressin to cause abdominal colic; a small dose of adrenaline caused anginal pain in one of the two patients. There were only slight changes in the pulse rate, blood pressure, metabolic rate, and cardiac output. It is therefore concluded that pitressin as used in the investigation can be given therapeutically without any risk of untoward cardiovascular results.

Pituitary gonadotrophic extracts

Antagonism to pregnant mare serum.—The preparation of two purified compounds of the pituitary gonadotrophic complex—the follicle stimulating hormone (F.S.H.) and the hormone which repairs the interstitial tissue of the hypophysectomized rat (I.C.S.H.), was reported by C. H. Li, Miriam E. Simpson, and H. M. Evans in 1939. Now H. L. Fraenkel-Conrat, Miriam E. Simpson, C. H. Li, and H. M. Evans find that the purest F.S.H. and I.C.S.H. fractions obtained from the sheep pituitary, when injected intraperitoneally in the lowest doses producing specific effects, antagonize the gonadotrophic effects of pregnant mare serum (P.M.S.) injected simultaneously. F.S.H. injected intraperitoneally was effective in both normal and hypophysectomized rats, in antagonizing the effect of the same substance injected simultaneously under the skin, when at certain dose levels. I.C.S.H. does not antagonize F.S.H. isolated from the pituitary of normal or hypophysectomized rats. The antagonism of I.C.S.H. to P.M.S. is easily seen, and it is even more striking that it does not antagonize P.M.S. in hypophysectomized rats. It is suggested that the antagonism of pituitary I.C.S.H. is exerted against the F.S.H. secreted by the pituitary of the test animal.

Promin

In streptococcal infection.—J. A. Toomey and F. E. Roach who treated more than 150 patients with promin found that, in equal dosage, it was less toxic than sulphapyridine, and in the dosage recommended did not cause haemolysis. It had a definite beneficial effect on streptococcal infections, especially those of the upper respiratory tract, and on erysipelas. A disadvantage is that it must be injected intravenously. An advantage is that it does not seem to produce crystals or concretions in the urinary tract.

Effect on experimental tuberculosis.—W. H. Feldman, H. C. Hinshaw, and H. E. Moses report the effect of promin, the sodium compound of bis (*p*-aminophenyl)-sulphone dextrose sulphonate, on experimental tuberculosis. Fifty adult male guinea-pigs were divided into (1) 30 guinea-pigs given promin by mouth and a subcutaneous injection of tubercle bacilli in suspension, and (2) 20 guinea-pigs given the suspension of tubercle bacilli only, as controls. That all the control guinea-pigs were dead by the eighty-second day, and 13 of the guinea-pigs treated by promin were alive after 164 days, shows that promin inhibits tuberculosis. Further, the severity of tuberculosis, when present in the treated animals, was very much less than in the controls. The possible effect of sulphathiazole on experimental tuberculosis in guinea-pigs has also been investigated. The results show that this compound has little, if any, effect on the expected course of the disease.

Blood levels.—J. A. Toomey and M. E. Dice report on the blood levels of promin, the sodium compound of bis (*p*-aminophenyl)-sulphone dextrose sulphonate, in 85 patients. A standard dose of 5 grammes of promin was given intravenously 3 times a day. Since patients showed clinical improvement after being given this dosage, the authors consider that the blood level produced, 4 to 10 milligrams per 100 cubic centimetres, should be satisfactory from a clinical viewpoint.

Thyroid extract

Reduction of bromine content of blood.—E. J. Baumann, D. B. Sprinson, and D. Marine found that the administration of thyroid extract, or excessive secretion of the thyroid gland, lowers the bromine content of the blood. This effect is probably due to the diuretic and stimulating action of thyroid on the kidney, which excretes more bromine. Glands which are hyperplastic as a result of a relative or absolute deficiency of iodine take up bromine instead. When iodine is supplied to animals with hyperplastic thyroids, they soon lose the accumulated bromine.

Intravenous Therapy

Pyrexial reactions

Bacterial and protein contamination.—F. A. Knott and B. Leibel mention the occurrence of pyrexial reactions complicating intravenous therapy, which may be due to the presence in the solutions employed of dead bacteria or traces of other foreign proteins or non-protein particulate matter. Foreign protein is the commonest cause. Dead bacteria or protein derivatives of them may be present as a result of faulty technique in distillation of water or sterilization of apparatus, or defects in worn-out apparatus. Solutions free from dead bacteria, but containing traces of protein capable of causing pyrexia, have been found to have an albuminoid-ammonia content ranging from 0.005 to 0.025 part per 100,000. This estimation is therefore useful in the detection and elimination of such contaminants.

Lanatoside C

Effect on heart

G. Fahr and J. LaDue found that lanatoside C, a stable crystalline glucoside derived from *Digitalis lanata*, did not cause any anatomical changes in the heart muscle of the dog when given in therapeutic doses daily for 3 months. Given intravenously to patients with auricular fibrillation, it reduced the heart rate to normal within 2 minutes to 2 hours. Orally it reduced the heart rate to normal in 24 to 48 hours. It was effective in the treatment of congestive heart failure if the normal sinus rhythm was present, and often restored normal rhythm in cases of supraventricular paroxysmal tachycardia and auricular flutter. It brought the pulse down to normal in some cases of auricular fibrillation associated with hyperthyroidism. It seems to be less toxic than preparations of *Digitalis purpurea*, and some patients who cannot tolerate the latter can take lanatoside C in effective doses.

Leptazol (Cardiazol)

Cardiographic changes

E. M. Kline, J. L. Fetterman, and G. H. Williams report their observations after 43 convulsions had been induced by leptazol (cardiazol), and after 9 injections of the drug in sub-convulsant doses. There was invariably a rise in both the systolic and the diastolic blood pressures and a change in the heart rate; the latter was inconstant in direction and in magnitude. The most striking disturbances were the frequent and varied arrhythmias which followed most of the convulsant doses and several of those which did not cause convulsions. These changes in the cardiac mechanism were probably the result of increased vagal tone and other factors such as asphyxia. After the convulsions the T waves of the electrocardiograms became tall and pointed, and the value of the Bazett systolic index (K) was greatly reduced. Permanent alterations of the cardiac mechanism did not occur.

Effect on psychomotor efficiency

J. J. O'Connell, C. M. Queens, and L. S. Penrose, as a result of tests of psychomotor efficiency in patients treated with leptazol (cardiazol), adduced some evidence that the drug increased psychomotor efficiency. This efficiency could not be directly due to the presence of the drug in the body, because the improvement persisted long after all the drug had been excreted. A general easing of psychomotor activity was apparently caused by the convulsions. The maximal benefit appeared to be produced by the first few treatments; thereafter the degree of improvement in response to each convulsant dose tended to decline. Patients who, before treatment, showed striking incompetence in tests of psychomotor activity, whether this was due to stupor or agitation, were those in whom the leptazol treatment was generally most effective. These patients also showed general physical improvement and gain in weight.

Liquid Paraffin

Absorption into tissues

The general belief that liquid paraffin, used as a laxative, is not absorbed into the tissues is questioned by W. A. Stryker. Previous experiments, based on quantitative analysis of the faeces and gross tissue analysis, substantiate the hypothesis that absorption does not occur. More delicate tests for the detection of small amounts of oil have given evidence of absorption. To confirm these, the author experimented on rabbits, rats, and guinea-pigs dosed regularly with oil. Sections of the intestine, mesenteric lymphatic glands, liver, and spleen were fixed

in Zenker's solution and stained with eosin and haematoxylin. The presence of liquid paraffin was indicated by large intracellular and extracellular vacuoles and giant cells, and confirmed by testing with sudan IV, orange sudan G and osmic acid (negative test). Vacuoles and giant cells were found in the intestine (rabbit only) and mesenteric lymphatic glands, though in the latter giant cells were often small or absent. Liver tissue contained vacuoles but no giant cells. Prominent macrophages were found in the spleen of the rat. Similar tests carried out on human necropsy material showed oil in the lymphatic glands in 60 per cent of the cases, oil in the liver in 16 per cent of the cases, and oil in the spleen in 24 per cent of the cases, but cases of oil in the intestine were not found. Chemical analysis based on a determination of the percentage of unsaponifiable fraction of the test and control tissues and the separation of the unsaponifiable components by chromalographic adsorption was done. There was a close correlation between chemical and histological findings.

Opiates

Effects on nervous system

According to H. G. Wolff, J. D. Hardy, and H. Goodall, the therapeutic efficacy of the opiates depends chiefly on the following three properties: (1) their threshold-raising action; (2) the dissociation of pain perception from the usual reaction to pain; (3) the induction of lethargy and sleep. In normal subjects the outstanding psychological effects of morphine are freedom from anxiety, feelings of contentment and relaxation, apathy, difficulties in mentation, lethargy, and sleep.

Penicillin

Chemotherapeutic properties

E. Chain, H. W. Florey, A. D. Gardner, N. G. Heatley, M. A. Jennings, J. Orr-Ewing, and A. G. Sanders investigated the properties of penicillin as a chemotherapeutic agent. A. Fleming (1929) had noticed that a mould produced a substance which inhibited the growth, particularly of staphylococci, streptococci, gonococci, meningococci, and other organisms, but not of *Bact. coli*, *H. influenzae*, *B. typhi*, *Ps. pyocyanea*, *B. proteus*, or *Vibrio cholerae*. He suggested its use as an inhibitor in the isolation of certain types of bacteria, especially *H. influenzae*. He also noted that the injection into animals of broth containing the substance, which he called penicillin, was no more toxic than plain broth, and he suggested that the substance might be a useful antiseptic for application to infected wounds. The mould is believed to be closely related to *Penicillium notatum*. From the culture medium a brown powder has been obtained which is freely soluble in water. Both it and its solution are stable for a considerable time and, although it is not a pure substance, its anti-bacterial activity is very great. E. Chain and his co-workers found that subcutaneous injection of solutions of penicillin into animals did not cause sloughing of the skin or any serious damage. Intravenous injections showed that the substance was only slightly, if at all, toxic for mice. No effects were observed on the blood pressure, heart-beat, or respiration of cats. *In vitro* experiments showed that the substance, in a dilution of 1 in several hundred thousand, inhibited the growth of *C. welchii* (two strains), *Cl. septicum*, *Cl. oedematiens*, *C. diphtheriae*, *Streptococcus pyogenes* (Lancefield, group A), *Streptococcus viridans*, *Streptococcus pneumoniae*, and staphylococci (three strains). Penicillin is not immediately bactericidal, but seems to interfere with multiplication. Therapeutic tests were made on mice infected with streptococci, staphylococci, and *Cl. septicum*. Repeated subcutaneous injections were then given. The mice infected with streptococci and staphylococci looked ill, some even appeared to be moribund, but as the experiment proceeded they progressively improved, until, at the end of 24 hours in the case of the streptococci, and about 36 to 48 hours in the case of the staphylococci, it was difficult or impossible to distinguish them from normal mice. The survivors of the *Cl. septicum* infection, on the other hand, remained well throughout, except for a few in which leg lesions appeared near the site of injection and cleared up in a few hours. The authors conclude that penicillin is particularly remarkable for its activity against the anaerobic organisms associated with gas-gangrene.

Percaine

Ocular sensitivity

C. A. Perera reports a case of local ocular sensitivity to nupercaine (percaine) employed as a local anaesthetic. This was the only case of sensitivity to the drug observed by the author in over 10,000 instillations. The reaction consisted of oedema of the eyelids and conjunctiva with itching of the eyelids.

Prostigmin Methylsulphate

Relief of pain

In combination with morphine.—D. Slaughter, J. C. Parsons, and H. D. Munal obtained excellent results in the relief of pain in various cases from the use of 1 cubic centimetre of a 1 in 2,000 solution of prostigmin methylsulphate together with one-half (8 milligrams) of the accepted dose of morphine. No untoward effects from the use of this combination were noted. Prostigmin methylsulphate relieves the tonic constipation caused by morphine, because it has a marked stimulant effect on intestinal peristalsis. The series of 100 patients treated included cases of trauma, post-operative pain, and coronary occlusion. This work appears to confirm the cholinergic action of morphine with regard to its effects on pain.

Quinocaine*In staphylococcal infection*

D. N. Ingram states that quinocaine, a local anaesthetic containing 0.648 per cent of quinine hydrobromide, gives much assistance in combating infections due to *Staphylococcus aureus*. The quinine hydrobromide content of this local anaesthetic gives a certain degree of protection against infection in clean operative wounds, by reason of its inhibiting effect upon the growth of most pathogens and upon the *Staphylococcus aureus* in a specific manner.

Rectal Administration of Drugs*Absorption and excretion*

Sodium salicylate used as test.—According to F. S. Nohara, rectal administration of drugs is preferable to oral; absorption is much quicker, as the drug cannot be influenced by gastric juices, and because it is absorbed into the vena cava directly. The author gave rabbits in controlled experiments sodium salicylate, rectally and orally respectively, and determined the sodium salicylate content of blood and urine after certain periods. The first traces of the drug were found in both animals after approximately the same time, but the maximal concentration in the blood was reached in 1 hour after rectal injection; on the other hand, after oral administration, it took 3 hours to reach the same level in the blood. The maximum concentration was higher by rectal than by oral application. The excretion after rectal administration was higher and faster than after oral application. The concentration of sodium salicylate in the urine due to rectal absorption after 1 hour was of the same value as that due to oral administration after 3 hours.

Reduction of Heat by Drugs*Treatment of cancer by antipyretic drugs*

The use of cooling by the administration of drugs in the treatment of cancer led J. B. Herrmann to investigate the cooling effects of morphine, paraldehyde, and nembutal (sodium pentobarbital) together with the effects of cold upon their toxicity. They were found to cause a temporary drop in temperature in rats exposed to a cold environment (3° C.). The maximum drop for morphine was 10° using 30 milligrams, for paraldehyde 3.5° using 3 cubic centimetres, and for nembutal 2.5° using 25 milligrams. Undrugged controls maintained constant temperatures. All three drugs became toxic when the room temperature was further reduced, and in most cases became lethal in small doses. Usually harmless doses of paraldehyde, 0.3 cubic centimetre, became lethal at 3° C. Nembutal (25 milligrams) was fatal to rats after 6 hours in the cold. Thirty milligrams of morphine sulphate per kilo were lethal after several hours at 3° C. Magnesium chloride causes a fall of temperature under exposure to cold and is eventually lethal. This has been interpreted as a depressant effect on the vegetative nervous system. Aspirin does not lower the body temperature on exposure to cold, but only when the subject is sensitized by fever.

Siccolam*Use in skin lesions*

H. C. Semon and F. Herrmann state that siccolam (zinc oxide 24 per cent, titanium oxide 21 per cent, and colloidal kaolin 8.5 per cent, made into a thick cream with a mixture of 1 part of glycerin and 2 parts of water) is a highly efficient antiphlogistic preparation, applicable in many inflammatory dermatoses, such as subacute and chronic eczema, neurodermatitis, seborrhoeic dermatitis, lichenoid exanthemata, toxic dermatitis, dermatitis herpetiformis, and intertriginous, dyshydrotic, or mycotic inflammations.

Silver Ferrihaemoglobin*In ophthalmic and oto-rhino-laryngological conditions*

R. D. Barnard reports on the use of silver ferrihaemoglobin in 373 patients with ophthalmic and oto-rhino-laryngological conditions in which silver is ordinarily employed. Satisfactory results were obtained in 73.4 per cent of cases. The preparation was found to be as effective as other silver protein preparations and to have in addition a greater degree of stability than other silver proteins towards light, solution, and electrolytes. It proved to be practically specific for Morax-Axenfeld conjunctivitis and gave excellent results in vernal conjunctivitis. Argrosis was not noted in any patient in whom it was used.

Sodium Diphenylhydantoinate*Effect of large doses*

C. D. Aring and M. Rosenbaum report the case of a young man who, on three occasions, ingested 60, 90.5, and 105 grains (3.5, 5.883, and 6.825 grammes) respectively of sodium diphenylhydantoinate over a period of minutes, 6 hours, and 10 hours. The chief symptoms were exhilaration, light-headedness, dizziness, nausea and vomiting, headache, staggering, diplopia, nystagmus, difficulty in converging the eyes, pupillary abnormalities, ataxia, tremor, and changes in reflexes. Of these, nystagmus persisted the longest, and was present for 8 days on the last occasion.

Sorbitol*As a dehydrating agent*

J. Browder and F. H. Bragdon describe the effect of sorbitol on the cerebrospinal fluid pressure, pulse, respiration, blood pressure, and psychological state in human subjects with and without disease of the central nervous system. A total of 50 intravenous injections of

50 cubic centimetres of a 50 per cent solution of sorbitol was given to 38 patients, 33 of whom had various intracranial lesions; the other 5 served as controls. Clinical improvement, as shown by a more lucid state of consciousness and relief of headache, was noted in 54 per cent of cases. In 4 of 5 patients in whom a rise in cerebrospinal fluid was noted, the injection of sorbitol caused an immediate reduction in pressure, followed by a secondary rise to a level higher than before the injection. The frequency of chills after the intravenous injection of this substance contra-indicates its use as a dehydrating agent.

Strophanthin and Glucose

Electrocardiogram changes

Hypertonic glucose injections in cardiac disease.—W. Hadorn finds that cardiac patients who show cardiac disturbance after ouabain (strophanthin) injections show the same disorder after hypertonic glucose injection. He therefore compares strophanthin injections with glucose injections in animals, to show their influence upon the electrocardiogram. Strophanthin injections alter the usual rabbit electrocardiogram, namely changes of P₁, prolongation of P-Q, changes of S-T and T; but in these, the individual properties of the myocardium are of greater importance than the dose of strophanthin. Addition of glucose to the strophanthin did not alter these results, and the addition of glucose did not increase the lethal strophanthin-glucose dose. The author has now given up the use of a mixed strophanthin glucose injection, and also glucose injections (hypertonic) as much employed in cardiac diseases. D. Scherf and J. Weissberg find that hypertonic glucose solution injected in cardiac disease causes severe pathological changes of the electrocardiogram, particularly in coronary diseases, although the treatment is useful when an osmotic effect, as in pulmonary oedema, is required. The author believes that the dangerous and harmful effect of hypertonic glucose injections is mainly due to the increased and abnormal insulin excretion caused by it, which in turn causes unusual adrenaline effects.

Sulphonamide Compounds

Absorption, excretion, and distribution

Sulphadiazine.—O. L. Peterson, E. Strauss, F. H. L. Taylor, and M. Finland report on the absorption, excretion, and distribution of sulphadiazine (2-sulphanilamidopyrimidine). It was found that higher blood levels were reached, and were more sustained, than with any of the other common sulphonamides. The conjugation of sulphadiazine in the blood is generally slight, and there is no tendency for the conjugated drug to be retained. The distribution of sulphadiazine in various tissues and between red blood cells and plasma is similar to that of sulphathiazole. In its penetration into the spinal fluid it resembles sulphanilamide and sulphapyridine. Sulphadiazine is not absorbed to any appreciable extent after rectal administration, and the sodium salt is only slightly absorbed. Nausea, vomiting, and mental depression are notably absent, and other toxic effects have not been noted. The therapeutic results in cases of pneumonia and other infective diseases indicate that the drug has considerable efficacy.

J. G. Reinhold, H. F. Flippin, L. Schwartz, and A. H. Domm, from investigation of the properties of 2-sulphanilamidopyrimidine (sulphapyrimidine, sulphadiazine), report that, when given in a single dose or in multiple doses by mouth to patients, its action resembles that of sulphapyridine more closely than that of sulphathiazole. Usually it is readily absorbed from the gastro-intestinal tract, is not excreted as readily as sulphathiazole, and disappears slowly from the blood. Smaller amounts of the sulphapyrimidine are required to maintain a given level in the blood. As regards toxicity, it appears at least to be no greater than that of other drugs of this group now employed in the treatment of pneumonia.

Sodium compounds.—E. Strauss, F. C. Lowell, F. H. L. Taylor, and M. Finland found that, in general, the sodium compounds of sulphanilamide, sulphapyridine, sulphathiazole, and sulphamethylthiazole, given intravenously or orally, produced higher blood levels, and that these blood levels were reached more rapidly than when the corresponding drugs were given by mouth. The highest levels were reached with sodium sulphathiazole. Sulphathiazole and its sodium salt were excreted more rapidly in the urine than either sulphanilamide or sulphapyridine. Sulphathiazole showed the least amount of conjugation and sulphapyridine the most. Sulphanilamide was fairly well absorbed by the rectum, whereas all the other drugs were poorly absorbed.

O. W. Barlow and D. R. Climenko find that the sodium salts of sulphapyridine and sulphathiazole are absorbed from the gastro-intestinal tracts of man and monkey more rapidly than their free salts. The simultaneous administration of alkali in the form of sodium bicarbonate or magnesium oxide with sulphathiazole hastens absorption of the drug from the human gastro-intestinal tract.

General action

Sulphathiazole.—G. Carroll, L. Kappel, and B. Lewis made a clinical investigation of sulphathiazole. The drug was administered orally in a dosage of 0.5 gramme every 6 hours for adults. The sodium salt was given intravenously, in a dosage of 1 gramme in 100 cubic centimetres of sterile distilled water. The powder was employed locally, being sprinkled generously in infected wounds or by insufflation into cavities. They employed the drug in 200 cases, including many forms of infection of the urinary tract. The drug was very effective against staphylococci, gonococci, and pneumococci. After its use in renal abscesses, carbuncles, furunculosis, osteomyelitis, septicaemia, ulcers of the penis, pyelonephritis, impetigo, and

other infections the patients recovered. Remarkable results were obtained in the treatment of lesions of the penis, on which the powdered drug was applied twice daily.

Sulphadiazine.—M. Finland, E. Strauss, and O. L. Peterson describe the treatment by sulphadiazine of 446 patients. Good results were obtained in the treatment of acute pneumonia (pneumococcal, staphylococcal, and streptococcal), other acute infections of the respiratory tract, pneumococcal meningitis, meningococcal infections, erysipelas, acute urinary infection, and acute gonococcal arthritis. Results were unsatisfactory in the treatment of chronic urinary infections, chronic gonococcal arthritis, subacute bacterial endocarditis, and chronic pulmonary infections. Other sulphonamides, however, were not more effective in these cases. The number of cases of each disease was not large enough to justify conclusive comparisons between sulphadiazine, sulphapyridine, and sulphathiazole except in pneumococcal pneumonia. For this disease sulphadiazine compared well with the other two. Moreover its toxic effects were few, and nausea and vomiting resulting from it were infrequent. The toxic effects of sulphathiazole were three times as numerous. Slight nitrogen retention occurred in a few cases, and the leucocyte count dropped early in some cases and in others fell between the eleventh and sixteenth day, returning to normal at the end of the treatment. There was 1 case of renal colic, haematuria, and anuria which was relieved by a catheter, and 9 cases of morbilliform eruptions. Renal and hepatic damage was checked in several patients and showed improvement in some cases. For severe cases sodium sulphadiazine in physiological saline solution was used. Concentrations of 1–5 per cent intravenously or of 0.5 per cent subcutaneously did not cause any ill effects.

W. H. Feinstone, R. D. Williams, R. T. Wolff, E. Huntington, and M. L. Crossley report on the toxicity, absorption, and chemotherapeutic activity of sulphadiazine (2-sulphanilamidopyrimidine). The acute toxicity of sulphadiazine for mice is about 175 to 200 milligrams per 100 cubic centimetres, as measured by the parenteral administration of toxic doses of the sodium salts of sulphathiazole and sulphapyridine and results in blood concentrations of about 80 and 65 milligrams per 100 cubic centimetres respectively. Sulphadiazine appears to produce less tissue damage in monkeys than does sulphathiazole or sulphapyridine respectively. The solubility of sulphadiazine in urine is much higher than that of the acetyl derivatives of sulphapyridine and sulphathiazole. The blood concentration from given doses of sulphadiazine is about four times as high in monkeys as is the concentration from similar doses of sulphapyridine. Sulphadiazine has a high therapeutic activity in experimental pneumococcal, streptococcal and staphylococcal, and Friedländer's bacillus-B infection in mice.

In Clostridium Welchii infection

Sulphanilamide.—G. A. Caldwell employed various methods of treating experimentally-produced compound fractures infected with *Clostridium welchii* in guinea-pigs. He found that débridement of the wounds, followed by implantation of sulphanilamide crystals and closure, led to survival of only 4 out of 19 animals.

Débridement of open wounds, followed by irrigation and the administration of 50 milligrams of sulphanilamide intraperitoneally, on the other hand, resulted in the survival of 7 out of 9 animals. Débridement and irrigation followed by implantation of zinc peroxide paste and suture led to the survival of 4 out of 5 animals. X-ray treatment had no effect on the progress of fulminating gas gangrene.

F. Hawking found that the application of sulphonamide compounds to experimental wounds infected with large numbers of gas-gangrene organisms saved a large proportion of the animals infected with *Cl. welchii* and *Cl. septique*, but had only a slight influence on *Cl. oedematiens* infections. Sulphathiazole was the most effective compound in all cases, and sulphanilamide was superior to sulphapyridine against *Cl. welchii*, but it had practically no effect against *Cl. septique*. The local application of sulphathiazole was more effective than intraperitoneal injection. The development of infection on these wounds can also be prevented by the administration of sera.

Sulphanilamides.—J. Gordon and J. W. McLeod, as a result of experiments in mice and guinea-pigs, conclude that the sulphanilamide drugs probably have only a limited value in the prophylaxis of gas gangrene, and that local administration is more valuable than oral. The drugs are not likely to be useful in treatment except in cases in which there is a mixed infection with a susceptible aerobe. In experimental work they are inferior to antisera in the prophylaxis of gas gangrene.

Action on Corynebacterium diphtheriae

Soluseptasine and M & B 693.—Although the mode of action of sulphonamide drugs on infections has attracted much attention, comparatively little has been done in the case of diphtheria. J. F. Murray of the South African Institute for Medical Research at Johannesburg has taken up this question. *In vitro* experiments with virulent strains of *Corynebacterium diphtheriae* show that a bacteriostatic action is exerted by M & B 693 soluble and by soluseptasine, the first-named being the more powerful. Different strains of *C. diphtheriae* vary in their susceptibility to the sulphonamides, but whatever the differences shown by 6 strains (4 of them *mitis*) of *C. diphtheriae*, there is a definite concentration of the drug, incorporated in the culture media, above which the bacteria consistently failed to grow. *In vivo* experiments showed that no protective or curative effect of the drug could ever be observed in susceptible animals inoculated with 24 hours culture of *C. diphtheriae*. The throats of a series of con-

valescent diphtheria patients were sprayed with a 1 in 50 aqueous dilution of M & B 693 soluble, but this failed to shorten the period required to obtain three successive negative swabs.

Pneumococcal infection

Effect on metabolism of pneumococcus.—R. A. McKinney and R. R. Mellon describe the effect of sulphonamides on the form and metabolic activity of the pneumococcus. Doses of less than the optimum therapeutic dose were injected regularly into mice with experimental pneumococcal peritonitis. Cultures of bacteria clearly distinguishable from the original strain were found, but were absent in the untreated controls. They represented a descending grade of metabolic activity measured by the fermentation of inulin, the production of hydrogen peroxide, and the degree of virulence. There was a serial disappearance of enzyme systems, suggesting that sulphonamides have an 'anti-enzyme' action. Morphologically the cultures grade from a modified mucoid colony to a minute, stable, non-virulent form. These types have their counterpart in the 'involution' forms *in vivo*, a designation criticized by the authors. The morphological and metabolic changes observed are reversible. One of the culture phases showed an increased susceptibility to phagocytes and underwent spontaneous autolysis, possibly due to metabolic disturbances. Sulphonamide-fast strains can be produced by subjecting the culture to gradually increasing doses of drug, but the immune form is merely an *in vitro* manifestation of one of the dissociative phases described.

Effect of sulphapyridine.—L. H. Schmidt, C. Hilles, H. A. Dettwiler, and E. Starks found that sulphapyridine was uniformly more effective against experimental infections with type I pneumococcus than against type III infections. Infections with certain type II strains responded as did type I, whereas infections with other strains responded as did type III. *In vitro* experiments showed that these type and strain variations were not related to differences in the bacteriostatic action of sulphapyridine. Nor were they due to retention of occasional organisms in isolated organs. It has been suggested that the differences in type and strain response were related to differences in antigenicity.

Staphylococcal infection

Sulphathiazole.—G. Carroll, L. Kappel, and B. Lewis find that sulphathiazole is a safe and effective agent in the treatment of staphylococcal infections of the urinary tract; it is readily absorbed when taken by mouth, and is excreted rapidly, chiefly by the kidneys. The usual dose is 4 grammes daily. The maximal amount given to any patient in 24 hours is 12 grammes, and the longest recorded period of continuous medication without subsequent deleterious effect is 50 days.

Sulphanilamide, sulphapyridine, sulphathiazole, sulphamethylthiazole, and neoarsphenamine.—E. E. Osgood, J. Joski, and I. E. Brownlee investigated the relative effectiveness of sulphanilamide, sulphapyridine, sulphathiazole, sulphamethylthiazole, and neoarsphenamine against *Staphylococcus aureus* infections, by the marrow-culture method. It was found that neoarsphenamine in concentrations of 1 in 150,000 to 1 in 200,000 was the most effective preparation. Sulphathiazole and sulphamethylthiazole, in concentrations of 1 in 10,000, were of definite value, but rarely led to complete sterility. Sulphapyridine was only slightly effective, and sulphanilamide was practically ineffective. The authors consider that the administration of neoarsphenamine in intermittent courses of repeated small doses, together with sulphathiazole in doses sufficient to give a blood concentration of 1 in 10,000 is worthy of controlled clinical investigation in serious *Staphylococcus aureus* infections.

Sulphamethylthiazole.—G. Carroll, L. Kappel, and B. Lewis, after employing sulphamethylthiazole in staphylococcal infections, state that the more seriously ill patients, all of whom recovered with sulphamethylthiazole treatment, failed to respond to sulphanilamide and sulphapyridine. The average dose of the drug is 6 to 12 grammes daily, but larger doses may be needed in deeply seated and extensive lesions. Patients who failed to respond promptly were found to have blood concentrations below 5 milligrams per 100 cubic centimetres; when the dose was increased and the concentration rose to 8 or 9 milligrams per 100 cubic centimetres, improvement occurred. In one case treated, peripheral neuritis was present.

Staphylococcal and streptococcal septicaemia

Sulphathiazole.—W. C. Stirling reports recovery in a case of staphylococcal septicaemia after the use of sulphathiazole, and in a case of non-haemolytic streptococcal septicaemia. In the first case the drug was given in an initial dosage of 4 grammes followed by 1 gramme every 6 hours for 4 days. A blood culture made after 5 days gave negative results. In the second case the same dosage was given, and by the second day the temperature became and remained normal. In both cases the origin of the infection was in the renal pelvis.

Dermatoses

Sulphapyridine.—H. MacCormac employed sulphapyridine with good results in 2 severe dermatoses. One was a case of extensive erythematous seborrhoeic eczema of the head, face, and ears, in a woman aged 32. After 4 courses of the drug with a total dosage of 43 grains, she was almost completely free from the eruption. The other case was chronic psoriasis with an attack of exfoliativa dermatitis. Within 14 days from the start of sulphapyridine therapy, the rash had entirely disappeared, except for a small patch under the chin.

In ophthalmology

Concentration in aqueous humour.—H. G. Scheie and B. F. Souders studied the penetration of sulphanilamide, sulphapyridine, sulphadiazine, and sulphathiazole into the aqueous humour of the eye after oral administration. The first was used in aqueous suspension and

was found in the aqueous humour at a concentration of 80 per cent of that in the blood. The second was used as a sodium salt and there was free penetration into the eye. Sulphadiazine showed good penetration, but there was a time lag in the aqueous level. The level of sulphathiazole in the eye was low and this drug cannot be considered of much value in the systemic treatment of eye infections.

Liver necrosis

Sulphanilamide investigated as possible cause.—T. E. Machella and G. M. Higgins, under the heading 'Does sulphanilamide induce necrotic lesions in the liver?', a subject on which divergent opinions have been expressed, report the results of the administration of the drug in suspension through a stomach tube, to healthy adult albino rats, for varying periods of time. The livers of rats receiving the drug were very dark in colour, and small in those given large doses. Necrotic foci were found in approximately 30 per cent of the rats so treated. Similar lesions, however, were present in 25 per cent of normal control rats of the same colony, age, and weight. The causation of these foci of necrosis in both the experimental and the control rats is not explained; but L. Buchbinder, L. Hall, S. L. Wilens, and C. A. Slanetz observed necrotic foci in the livers of apparently normal adult rats from which paratyphoid bacilli were cultivated, and pointed out that an enzootic type of paratyphoid infection may be so mild as to escape notice.

Rectal administration

Sulphanilamide.—E. H. Wood finds that the rectal administration of sulphanilamide causes fewer complications than injection by other routes. He advises this route for the general practitioner who has not any first-class hospital facilities, or for the benefit of the patient who cannot take the drug by mouth. The rectal solution employed is 1 per cent glucose in normal saline. A saturated solution of sulphanilamide is prepared; each ounce of decanted fluid contains about 4 grains of the drug. When giving a dose of the drug this is made up to a total volume of 40 ounces by adding the glucose-saline solution.

Reduction in tissue suspensions

Neo-prontosil.—F. Bernheim reports on the reduction of neo-prontosil by certain tissues *in vitro*. A suspension of rat liver incubated semi-anaerobically reduced the dye. Under the same conditions kidney caused comparatively little reduction, and brain and muscle none at all. The addition of cystine, thioglycolic acid, or ethyl alcohol increased the reduction rate of liver, but had little effect with kidney or brain. As muscle was also inactive, the results of these experiments indicate that neo-prontosil is reduced almost exclusively in the liver.

Renal complications

Sulphathiazole.—C. F. Garvin found that 33 (61.6 per cent) of 54 patients with pneumonia treated with sulphathiazole showed crystals of the drug in the urine, in contrast to 16 (28.6 per cent) of 56 patients treated with sulphapyridine. This difference can probably be explained by the fact that 10.1 grammes of sulphathiazole daily were required to produce a blood level of 5.8 milligrams per 100 cubic centimetres, whereas 5.1 grammes of sulphapyridine were sufficient to maintain a concentration of 5.4 milligrams per 100 cubic centimetres. The incidence of haematuria was 14.8 per cent for the group treated with sulphathiazole, and 10.7 per cent for sulphapyridine.

Toxic reactions

Sulphamethylthiazole.—It is known that toxic reactions caused by sulphamethylthiazole resemble those caused by sulphanilamide and sulphapyridine. In addition peripheral neuropathy has been reported to result from sulphamethylthiazole therapy, and C. F. Garvin has reported a case in which peripheral neuropathy was associated with a toxic psychosis. The patient, a negress aged 37, was admitted to hospital with pneumonia; a temperature of 104.2° F.; pulse 145; respirations 45 per minute; red cell count 4,000,000; white cell count 9,300 per cubic centimetre with 82 per cent neutrophils; albuminuria; and negative Wassermann but positive Kline tests. Pneumococcus Type XIV was present in sputum and blood. Sulphamethylthiazole was administered, beginning with an initial dose of 4 grammes; subsequent doses were given at intervals of 4 hours. The total daily dosage was: first day 6 grammes, second to fifth days 12 grammes, sixth to sixteenth days 6 grammes, and seventeenth day 5 grammes, making a total of 125 grammes. The concentration of the drug in the blood varied between 1.9 milligrams per 100 cubic centimetres on the second day to 5 milligrams per 100 cubic centimetres on the fifteenth day. Digitalis was administered for auricular fibrillation. Thiamin chloride was also given, but in spite of this there were signs of peripheral neuropathy on the seventeenth day and the sulphamethylthiazole was therefore stopped. The next morning the patient had 2 generalized convulsions and during the next 3 days she had 12 such convulsions and became unresponsive and stuporous. She died on the twenty-fourth day after the beginning of treatment. Necropsy indicated that the patient died of toxic psychosis which is ascribed by the author to the use of sulphamethylthiazole.

Sulphapyridine.—The occurrence of agranulocytosis and severe haemolytic anaemia is known to follow sulphapyridine therapy. H. K. Russell and R. C. Page now report 2 cases of thrombocytopenic purpura, one of which ended fatally, after administration of sulphapyridine. In the first patient, a negro aged 41, X-rays showed pneumonitis of the left lower lobe and a cavity in the left upper lobe; acid-fast bacilli were found in the sputum, but not pneumococci. On admission his blood sulphapyridine was 2.9 milligrams per 100 cubic centimetres. During the first 10 days in hospital he received 4.5 grammes daily of sulpha-

pyridine; the drug was then discontinued as haemoptysis and recurrent epistaxis developed. On the eleventh day a generalized purpura was added to these symptoms and oozing from the gums. A diagnosis of thrombocytopenic purpura was made. He was treated by blood transfusions but the purpuric manifestations continued and 10 weeks later progressive jaundice developed. This subsequently disappeared and the patient recovered.

The second patient was an Italian man of 60 in whom an X-ray diagnosis of lobar pneumonia was made. He was given sulphapyridine, 18 grammes spread over 4 days. The temperature dropped to normal and the drug was discontinued, but as the temperature rose again, sulphapyridine was again given, 5 grammes during 3 days. The total amount of the drug administered was therefore 23 grammes. Sputum culture showed a few pneumococci, 60 per cent *Staphylococcus albus*, and 30 per cent haemolytic streptococci; throat culture showed 70 per cent haemolytic staphylococci and 30 per cent haemolytic streptococci. On the eighth day in hospital the patient had purpuric manifestations and epistaxis, and the following day bleeding from the gums and oral mucous membranes. A diagnosis of thrombocytopenic purpura was made and the patient was given 3 transfusions totalling 1,700 cubic centimetres of whole blood. He also received ascorbic acid and intravenous injections of oxalic acid, 5 milligrams twice daily, but in spite of this he died 14 days after admission. On the day of his death the bleeding time was 3 hours 4 minutes and blood platelets could not be found in stained smears.

Sulphanilamide causing secondary anaemia.—A. P. Richardson found that the continued administration of sulphanilamide in the diet of mice produced a secondary anaemia closely resembling that from clinical medication. The anaemia was characterized by reticulocytosis, increase in the mean corpuscular volume of erythrocytes, development of Heinz bodies, and marked deposits of haemosiderin in the spleen; the leucocytes and the platelets were unchanged. A given concentration of the drug produced maximal blood changes within 2 to 4 weeks, beyond which period continued administration of the drug produced no further anaemia. Splenectomy had no effect on the development of anaemia or cyanosis.

Sulphathiazole.—E. Strauss and M. Finland find that *p*-aminobenzoic acid is unable to resolve or prevent the fevers and rashes due to sulphathiazole, even when it is given in amounts sufficient to counteract the anti-bacterial action of the sulphonamide compound in the blood and urine. This contradicts the suggestion of Fildes (1940) that administration of *p*-aminobenzoic acid might overcome the toxic effects of sulphonamide compounds.

Agranulocytosis in an infant.—H. C. Barlow reports a case of agranulocytosis in a female infant aged 1 year and 11 months, after the administration of sulphapyridine, a total of 1½ grammes being given during 5 days, for febrile inflammation of the right membrana tympani. On admission to hospital, before any sulphonamide was given, the patient was profoundly anaemic, with red cells under one million and haemoglobin 18 per cent. At first the blood picture seemed to suggest an aleukaemic lymphocytic leukaemia and for several days not a single granulocyte could be found. A great improvement in the condition occurred after the first blood transfusion. Pentnucleotide was also given and the child made a complete recovery.

Rash.—A. M. Greenwood points out that rashes in the course of sulphonamide therapy are multifactorial in character, and are not specific, with the possible exception of those appearing after the use of sulphathiazole, that they may be manifestations of toxæmia, sensitization, or allergy, that they may occur at any time during treatment, but generally from the fourth to the fourteenth day, and in from 2 to 30 per cent of the cases, depending on the intensity of treatment. They are more likely to appear in areas exposed to sunlight, and may be accompanied by an increase in the excretion of porphyrins.

I. F. Volini, R. O. Levitt, and H. B. O'Neil report 2 cases of cutaneous eruptions and conjunctivitis due to sulphathiazole therapy. The rashes due to the drug are urticarial, erythematous, macular, papular, nodular, and purpuric. The nodular eruption is the most characteristic and has been associated with a fatal outcome in a high percentage of cases. There is not any correlation between the level of the drug in the blood and the development of the rash. Most rashes occur on the fifth day, or later. Conjunctivitis is frequent. When these rashes occur, the administration of the drug should be stopped.

Tropical diseases

K. V. Earle, discussing the use of the sulphonamide compounds in some tropical conditions, reports that the drugs are of little value in dengue and ulcerative granuloma. Good results were obtained in lymphopathia venereum and in tropical pyomyositis. The secondary streptococcal infection in fungous diseases clears up on their administration.

Urinary infections

Sulphathiazole and sulphanilamide.—H. F. Helmholz, in an article on the effect of minimal doses of sulphathiazole on chronic urinary infection with high blood urea, describes the case of a boy, aged 16 years, who for at least 14 years had been the subject of chronic urinary infection and had been treated by methenamine, ketogenic diet, mandelic acid, sulphanilamide, and sulphathiazole. Doses of sulphathiazole of 0.25 gramme 6 times, 4 times, and 3 times a day had untoward effects on this boy, such as fainting and convulsions, and it was found that very small doses, 0.125 gramme (2 grains) in the 24 hours, were well tolerated and most effective in clearing the urine of bacteria. H. F. Helmholz and Norah Larson compare the bactericidal effect of low urinary concentrations of sulphanilamide and sulphathiazole on bacteria from urinary infections. The urine of patients taking the drugs was used for testing

the 85 strains of various bacteria. These observations showed that sulphathiazole is definitely superior to sulphanilamide as a urinary antiseptic in concentrations of from 10 to 30 milligrams per 100 cubic centimetres of urine as determined by experiments *in vitro*. The bactericidal action of sulphathiazole in concentrations of 10 milligrams per 100 cubic centimetres of urine brings it well within the range possible for therapeutic use for urinary infections when the kidneys are damaged; in such cases dosages of 0.3 to 0.65 gramme (5 to 10 grains) should be tried.

Sulphathiazole.—H. F. Helmholz describes the results of experiments to determine the effective bactericidal concentrations of sulphathiazole for common urinary bacteria. At 5 milligrams per 100 cubic centimetres of urine *Staphylococcus aureus*, *Proteus ammoniae*, *Salmonella*, *Aerobacter aerogenes*, and *Escherichia coli* were all affected in a high percentage of tests. The last was affected in 92 per cent of the tests. *Pseudomonas aeruginosa*, however, is not affected at this concentration and in 15 per cent of the tests required a double-strength concentration. An ample concentration for an efficient urinary antiseptic should thus be 10 milligrams per 100 cubic centimetres. *Escherichia* is the organism usually found in the urine of a patient with post-operative urinary stasis. A daily dose of 0.65 gramme of sulphathiazole orally produces a urine concentration of 20–30 milligrams per 100 cubic centimetres and should be given to patients before and after catheterization.

H. F. Helmholz and Nora Larson report on the bactericidal effect of sulphathiazole on 20 strains of *Escherichia coli*, 14 strains of *Aerobacter aerogenes*, 10 strains each of *Proteus ammoniae*, *Pseudomonas aeruginosa*, and *Streptococcus faecalis*, and 5 strains of *Staphylococcus aureus*. The total number of series of observations was 2,003, and in order to estimate the bactericidal effect at different levels of alkalinity and acidity, the observations were made at pH 5.5, 6.5, and 7.5, and the urine from a number of patients taking sulphathiazole in doses from a half to two-thirds the usual doses for respiratory infections. Sulphathiazole was found to be bactericidal for six of the most common urinary infections, and a concentration of 300 milligrams per 100 cubic centimetres should cure practically all the infections. The efficacy for the various bacteria in an ascending scale was as follows: *Pseudomonas aeruginosa*, *Streptococcus faecalis*, *Escherichia coli*, *Aerobacter aerogenes*, *Proteus ammoniae*, and *Staphylococcus aureus*. The *Pseudomonas aeruginosa* is one of the most difficult to get rid of from urinary infections; the pH does not seem to play any part. A recent infection yielded rather rapidly to sulphathiazole when a concentration of more than 300 milligrams per 300 cubic centimetres was maintained in the urine for 5 days. The drug is bactericidal even in low concentration for *Streptococcus faecalis*, against which sulphanilamide is ineffective. It seems most active in low concentration against *Staphylococcus aureus*, and then against *Proteus ammoniae*.

O. C. Culp treated 30 patients with urinary tract infections with sulphathiazole. In 24 cases an attempt was made to sterilize the urine completely, and in 16, 66.7 per cent, of these all infection was eliminated. Three patients had recurrences after sulphathiazole was stopped, due to a pre-existent calculus in 1 case and to chronic prostatitis with residual urine in the other 2 cases. In 4 other cases with mixed infections, all organisms disappeared except gamma *Str. faecalis*. Organisms which were killed by sulphathiazole in this series of cases were *Staph. albus*, *Staph. aureus*, proteus, escherichia, aerobacter, *C. xerosis*, and alpha *Str. mitis*. The most resistant organism was *Str. faecalis*. The drug was given to 6 patients only during acute pyelitis, and in all with rapid symptomatic improvement. The dosage in most cases was 1 gramme of the drug, every 6 hours for 5 to 10 days. Of the entire group of patients, toxic manifestations, such as conjunctivitis, dermatitis, fever, nausea and vomiting, and anaemia, occurred in 23.3 per cent. The author concludes that sulphathiazole is an excellent urinary antiseptic, if administered under favourable conditions and with great care.

Sulphanilamide.—Two articles on the prophylactic use of sulphanilamide in the control of post-operative infection of the urinary tract have appeared as the result of observations made during 9 months at the Mayo Clinic on 514 patients. The first article, by J. L. Emmett and H. J. Hammer of the section of urology, deals with cases mentioned above as operated upon by R. B. Wilson and J. C. Masson who contribute the other article. The object of the first article is to determine whether or not the post-operative administration of sulphanilamide controls urinary infection in a sufficiently large percentage of cases to justify its routine use in general surgery. Post-operative urinary infection occurs especially when catheterization has been necessary, and this is prone to occur after some operations, particularly gynaecological, near the bladder. It has been suggested that the danger of catheterization is less in its technique than in urinary stagnation, and the injury to the vesical mucosa, produced by over-distension of the bladder is the most important factor in the production of post-operative cystitis (Cabot). Among the 514 cases catheterization was performed in 262, and in only 197 of these was the condition of the urine followed up after discharge from the hospital, and therefore the following figures are based on the results obtained in the 197 cases: of the 73 patients receiving the complete prophylactic treatment by sulphanilamide the incidence of urinary infection was about 18 per cent, as compared with an incidence of 50 per cent in the control group of patients who did not receive the treatment. Among 115 cases in which a retention catheter and intermittent catheterization were employed and in which the most severe post-operative urinary infection would be expected, the incidence of infection among patients receiving the complete prophylactic course was 25, whereas in the control cases it

was 72.5 per cent. This result is encouraging; but Wilson and Masson suggest that pre-operative prophylactic treatment might appreciably diminish the incidence of post-operative urinary infections. A high percentage of failures of the prophylactic treatment occurred in cases of infection by *Streptococcus faecalis*. As it had been suggested that sulphathiazole might be more effective, it was tried in a number of cases, but seemed to be inferior to mandelic acid preparations.

Urinary tract complications

Sulphathiazole.—S. A. Loewenberg, N. G. Sloane, and P. Chodoff found concretions in the urinary tract of a patient treated with sulphathiazole for pneumonia. In this case the drug had no effect on the pneumococcaemia or on the acute bacterial endocarditis. At necropsy the renal calyces and pelvis, the ureters and bladder contained numerous bright orange-coloured irregular shaped calculi measuring from 1 to 2.5 millimetres.

Sulphapyridine.—H. M. Spence reports the case of a man, aged 69, in whom haematuria, renal colic, and complete anuria occurred after the use of sulphapyridine for lobar pneumonia. After receiving a total of 165 grains (11 grammes) of the drug, he had severe right renal colic, and passed 60 cubic centimetres of urine containing blood. Within a few hours anuria followed, and the bladder was empty when the catheter was used. After 18 hours of complete anuria, a cystoscopy was carried out and concretions were found in both ureters. Ureteral catheters were left in place for 72 hours, and thereafter the urine was passed normally and the patient recovered.

Sodium compounds.—W. Antopol, D. Lehr, J. Churg, and H. Sprinz describe the changes in the urinary tract after the administration of sodium sulphapyridine, sodium sulphathiazole, and sodium sulphamethylthiazole. They found a high incidence of intrarenal precipitation and urolith formation, accompanied by severe damage to the kidneys and liver after sodium sulphamethylthiazole. The administration of large doses of sodium sulphathiazole is always succeeded by acute massive precipitation of the free drug in the urinary tract. With chronic administration renal concretions can be produced with each of the three compounds, and are due to the formation of the very insoluble acetylated derivatives of these compounds. There is generally calcifying nephrosis of varying degrees, chiefly of the convoluted tubules.

Sulphur-containing substances and sulphonamides

Sulphur-containing compounds, such as magnesium sulphate and other saline purgatives, eggs, and pentothal sodium (which contains 12 per cent of sulphur), have been forbidden to patients receiving sulphonamide therapy, on the grounds that they are likely to cause sulphaemoglobinaemia and cyanosis. E. J. R. Smith reports on 30 surgical patients on whom up to 1.75 grammes of pentothal sodium was used as an anaesthetic, and to whom sulphapyridine was given orally or intravenously at the time of operation or within 3 days of operation. Not in any case was a trace of cyanosis observed. The author has also dehydrated patients by oral or rectal magnesium sulphate during sulphapyridine medication without untoward results. He doubts if it is necessary to exclude eggs from the dietary of patients receiving sulphapyridine.

Sympathomimetic and Parasympathomimetic Drugs

Intravenous drip administration

A. Myerson and J. Loman state that the sympathomimetic drugs benzedrine, paredrine, and propadrine hydrochloride may be given by the intravenous drip method for a prolonged period. A rise in blood pressure to a desired level can be easily reached, and can be maintained indefinitely. The parasympathomimetic drugs, acetyl-beta-methylcholine chloride and furfuryl trimethyl ammonium iodide, can also be given by this method. Clinically the sympathomimetic drugs can be added to fluids given during the course of operations when it is desirable to increase or prevent a fall in blood pressure. Benzedrine might be employed by the drip method in the treatment of barbiturate poisoning.

Thiocyanates

Toxic effect

Pathology.—H. A. Lindberg, M. H. Wald, and M. H. Barker report the effects of prolonged administration of toxic doses (5 grains, 0.3 gramme) of potassium thiocyanate by mouth to 12 normal dogs. The blood picture showed a severe microcytic anaemia, with diminution of the red count, the haemocrit value, the blood cholesterol, and total serum proteins. The polymorphonuclear leucocytes, the other granular cells, and the reticulocytes were normal. There was no jaundice or haemosiderosis. Biopsy of the sternum, rib, and femur showed a relatively non-cellular bone-marrow. In the milder cases the place of the normal matrix was taken by fat, and in the more severe cases instead of the normal fatty marrow there was clear light eosin-staining gelatinous material. The liver showed intracellular fatty vacuolization. The adrenals were free from any morbid changes, and the authors cannot accept the suggestion that hypoadrenia may be the chief feature of the toxicology of the thiocyanates. In connexion with the use of thiocyanates in the reduction of high arterial blood pressure it is pointed out that the vasodilatory effect is observed long before the altered blood picture and other changes, if indeed they occur at all. The properly controlled hypertensive patients should be given only a quantity of thiocyanates sufficient to maintain blood concentrations considered safe (8 to 14 milligrams per cent), whereas very toxic amounts (20 to 60 milligrams per cent) were given to the 12 dogs.

Trasentin and Trasentin-6H*Toxicity*

J. D. P. Graham and S. Lazarus, investigating the actions of trasentin and trasentin-6H, found that the toxicity (lethal dose 0.50) by intraperitoneal injection in white mice of trasentin (the hydrochloride of the diethylaminoethyl ester of diphenylacetic acid) is 0.29 gramme per kilo, and of trasentin-6H (diethylaminoethyl ester of phenylcyclohexylacetic acid) is 0.24 gramme per kilo. The toxicity of atropine sulphate is 0.325 gramme per kilo. Trasentin is a convulsant and respiratory stimulant in sub-lethal doses, and trasentin-6H exerts the same effects in doses of 1 in 5 millions, and is a more powerful spasmolytic. In the rabbit under ether anaesthesia and in the spinal cat, the tone and movements of the intestine are inhibited by 0.01 to 0.02 milligram per kilo of trasentin-6H, and 0.1 milligram per kilo of trasentin. The stomach and bladder of the cat are relaxed by 0.05 milligram per kilo of trasentin-6H. The latter drug is about 25 per cent more toxic than atropine sulphate, but has a proportionately greater spasmolytic action. As it is relatively free from side effects, it appears to be worthy of clinical trial.

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PHARYNX DISEASES

See also B.E.M.P., Vol. IX, p. 570; and Surveys and Abstracts 1939, p. 90; 1940, p. 463.

Acute Pharyngitis and Vincent's Angina*Unusual type*

B. B. Breese, Jun. describes the characteristics of an unusual type of pharyngitis of unknown aetiology, which he called aphthous pharyngitis, observed in 28 patients. There was a sudden onset of high fever, occasional attacks of moderate vomiting, acute inflammation of the throat without much local soreness, disappearance of the fever in 24 hours, and the appearance, often coincident with the drop in temperature, of a few discrete aphthous or canker-sore-like lesions on the upper portions of the tonsillar pillars. The incubation period was about 3 days.

Tumours of the Pharynx*Clinical picture*

Polypoid fibro-lipomatosis pharyngis.—R. Smith reports a case of polypoid fibro-lipomatosis pharyngis in a man aged 81. The notable features of this case were its rarity; the variation of the symptoms according to the relation of the tumours to the important food and air passages; the surprising size of the growths tolerated in the lumen of the oesophagus without causing any symptoms when the polypoid mass has entered the oesophagus; and the attacks of dysphagia which were followed by symptom-free intervals.

Carcinoma of the tonsil

General review.—In their monograph on cancer of the tonsil H. Martin and E. L. Sugarbaker deal with 157 unselected consecutive cases including all patients in all stages of the disease who applied to the Memorial Hospital, New York, during the years 1931–5, and thus follow J. J. Duffy who reported on the cases of tonsillar carcinoma for the years 1920–30. The title of cancer of the tonsil does not include the pharyngeal and lingual tonsils. The lymphatic drainage of the palatine tonsil passes directly outwards to the sub-digastric lymphatic glands of the jugular chain, which are involved in 95 per cent of tonsillar metastases. Of the pharyngeal structures, cancer of the tonsil (21 per cent) is second only to the extrinsic larynx as the site of origin of malignant tumours. Among the 157 cases the average age was about 57, the extremes being 94 and 11 years. Males were attacked in 86 and females in 14 per cent, the age incidence being the same in the sexes. The right tonsil was affected in 60 per cent. About 70 per cent of the patients were smokers but, as in other forms of intra-oral cancer, this percentage is found in normal male adults of corresponding age and does not appear to be significant. Clinically the first symptom was pain, in 60 per cent, and the second the patient's complaint of an enlarged gland in the neck, in 33 per cent. In less than 10 per cent was there complaint of a lump in the throat, dysphagia, or cough. An early case usually presents a superficial granular ulcer either on the tonsil or in the groove between it and one of its pillars. As in all cancers of Waldeyer's tonsillar ring, metastases play an early and important part. On admission clinically demonstrable cervical metastases were present in 76 per cent of the cases; in 36 cases (25 per cent of the determinate group) there was not any evidence of metastasis on admission, and the disease was permanently controlled; in 17 cases (11 per cent of the determinate cases) the patients died of uncontrolled cancer of the tonsil without any metastases after an average duration of 19 months. As the question of the validity of the diagnosis of metastases might be raised, it is pointed out that in the Head and Neck Department of the Memorial Hospital all cases of demonstrable metastases are subjected to aspiration biopsy. Dissemination below the clavicle is rare; in the necropsy records of the Memorial Hospital among 29 patients examined after death from cancer of the tonsil there were 3 only with visceral metastases (mediastinum, stomach, bones). The only explanation suggested is that the patients do not live long enough. Of the 157 cases 120, or 84 per cent, were epidermoid carcinoma (4 grades of squamous-celled carcinoma, 1 group of ungraded squamous-celled carcinoma, and 4 grades of transitional-celled carcinoma, namely, without keratinization). Lymphosarcoma occurred in 16 per cent of the cases. The term lympho-epithelioma, introduced by Regaud and later used by Schmincke, is regarded as unsatisfactory as it has been used in different senses; some of such cases are here called lymphosarcoma. Surgical removal of tonsillar cancer has been most disappointing and the authors consider that Despons's epithet of 'the surgery of despair' is justified. Tonsillar cancer is one of the most radio-sensitive of the oral and pharyngeal growths. Minor salivary gland tumours, resembling the mixed parotid tumours, have been seen in the tonsils, though not in this series, at the Memorial Hospital; they are highly radio-resistant, and should be

enucleated preferably by cautery and blunt dissection. Cancer of the tonsil is now treated at the Memorial Hospital by submaximal doses of fractionated X-radiation, supplemented in most cases by the implantation of small doses of radon seeds in the residual tumour, either directly into the primary lesion or in immediately adjacent metastatic lymphatic glands. The acute and chronic effects of powerful X-irradiation are fully described and methods of alleviation recommended.

Ulcers

Clinical picture

Decubital ulcers.—R. Waldapfel states that the condition called by T. Heryng, in 1890, 'benign ulcers of the pharynx', should be called decubital ulcers of the pharynx. He explains the mechanics of the development of these ulcers as follows: the ulcer appears in the area where the opposing tonsillar swellings and the base of the tongue constantly press on the mucous membrane of the anterior pillar, which lies between them. If the uvula is much swollen, such an ulcer may occasionally develop also on the uvula.

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PHYSIOTHERAPY

Its Uses in General Practice

H. S. Hoffman lays stress on the importance of physiotherapy to the general practitioner in various situations. It may be employed as a specific treatment in conditions of known aetiology; as supplementary treatment of diseases of known cause and specific non-physical treatment, or in diseases of known cause without any specific treatment; as a specific treatment in conditions of unknown aetiology and as an adjuvant in conditions of unknown aetiology without any specific treatment. It is essential that the practitioner should know the principles underlying the theory and application of physiotherapy although he need not be an expert in the handling of equipment. The inclusion of physiotherapy graduate and post-graduate medical courses is strongly urged. For the practitioner an ultra-violet light, high frequency machine, a source of galvanic and faradic current and an infra-red lamp constitute adequate equipment so far as America is concerned. Procedure, however, is generally lengthy and it is advisable to employ a trained assistant.

General and Local Refrigeration

M. K. Newman and J. M. Berris treated 11 patients with advanced metastatic carcinoma and 3 morphine addicts by general refrigeration, and 6 patients with metastatic carcinoma by local refrigeration. Treatment varied from 8 to 120 hours at temperatures below 88° F. These observers found that relief of pain occurred for varying periods. Regressive changes in growths were noted with local refrigeration. Morphine addicts appeared to respond favourably to general refrigeration.

Hoffman, H. S. (1941) *Physiotherapy Rev.*, **21**, 139.

Newman, M. K., and Berris, J. M. (1941) *Arch. phys. Ther.*, **22**, 161.

PINEAL BODY, TUMOURS

See also B.E.M.P., Vol. IX, p. 598; and Surveys and Abstracts 1939, p. 474.

Pineal Tumours

Clinical picture

J. Martin and L. Davis report the results of pinealectomy in experimental animals. The gland was destroyed electrically in young cats, dogs, and rats which were observed with controls for 4½ years. Pinealectomized females gave birth to premature feeble young, the milk glands were undeveloped and only responded slightly to prolactin. Pinealectomized males were sexually precocious and of larger size. Second generation animals were difficult to rear, prone to infection, and had a high mortality rate and the males were sexually precocious. Eighteen human patients with pineal tumours were also observed. The common symptoms were headache, blurred vision, diplopia, ataxia, drowsiness, changes in the pupils, transient convulsions, disturbances of heat and water regulating centres, permanent paralysis of orbital muscles, and later, papilloedema, weakness, spasticity, low temperature, and low metabolic rate. Boys of pre-puberal age showed precocious sexual and somatic development. All the 4 female patients had amenorrhoea, but one had a normal child. Other symptoms found at a late stage were polydipsia or polyuria alone, polyphagia, subnormal temperature, cachexia, apathy, infantilism, obesity, somnolence, skin pigmentation, and hypotension. These symptoms are probably due, not to the pineal tumour alone, but to lesions in other regions of the brain secondary to overgrowth of the tumour. They were not found in the experimental animals.

Martin, J., and Davis, L. (1941) *Arch. intern. Med.*, **67**, 1119.

PITUITARY GLAND DISEASES

See also B.E.M.P., Vol. IX, p. 611; and Surveys and Abstracts 1939, pp. 108 and 47 1940, p. 464.

Anatomy and Physiology*Physiology*

Purified interstitial cell-stimulating pituitary hormone.—C. H. Li, M. E. Simpson, and H. M. Evans describe a method of purification of this hormone and of some of the physico-chemical properties of this product. While this paper was in the press an article on the isolation of the pure form of the interstitial cell-stimulating (luteinizing) hormone of the anterior lobe of the pituitary gland appeared by T. A. Shedlovsky, R. O. Rothen, H. B. Greep, H. B. Van Dyke and B. F. Chou. Both papers report the preparation of an apparently pure protein with similar biological properties, the minimal effective dose (M.E.D.) also being the same. In an addendum to their paper, Li, Simpson, and Evans point out a considerable difference between the two proteins described, which may be due to several factors: (1) the preparation from the pituitaries of sheep by Li, Simpson, and Evans, and of swine by Shedlovsky, Rothen, Greep, Van Dyke, and Chou; (2) the wide differences in the early stages of the methods employed; (3) the pure protein of either laboratory may be an inert protein, contaminated with physico-chemically undetectable amounts of the actual hormone; and (4) the new method of assay used by Shedlovsky and his collaborators which employs a criterion different from that of Li, Simpson, and Evans, being based on maintenance rather than on repair of the interstitial tissue. In a further note on this subject Li, Simpson, and Evans emphasize these differences and conclude that, although proteins with similar biological properties have been isolated by two laboratories, the results from electrophoretic studies are so different as to forbid identification of the substances in question.

Growth hormone.—In a paper entitled 'Further Purification of the Growth Hormone of the Anterior Pituitary', H. L. Fraenkel-Conrat, D. L. Meamber, M. E. Simpson, and H. M. Evans point out that although experimentally produced overgrowth and undergrowth of the body has given convincing evidence of the endocrine control of growth by the anterior pituitary, the existence of a growth hormone as a specific chemical entity has been challenged. The undoubted increases in body weight and dimensions after the administration of some anterior pituitary extracts have been regarded as additive or synergic effects from other specific pituitary hormones. In a preliminary note H. M. Evans, N. Uyei, Q. R. Bartz, and M. E. Simpson (1938) showed that by the action of cystine alone it was possible to inactivate or remove most of the gonadotrophic, thyrotrophic, and lactogenic activity from such globulin fractions, leaving the growth-stimulating activity unimpaired (Meamber, Fraenkel-Conrat, Simpson, and Evans, 1939). In their latest article these authors report a simplified method of extraction of growth hormone, and give details of the application of cystine for the purification of this hormone, describe an investigation of some of the physico-chemical and biological properties of cystine-treated growth hormone, and in a footnote refer to the new criterion for estimating growth, namely, increase in the tail length of the hypophysectomized rat (Freu, Levie, and Kroon, 1939); this criterion, however, was not satisfactory in the authors' hands because the tails of their colony of rats grew for a limited time after hypophysectomy. The experiments showed cystine-treated extracts of anterior pituitary removed thyrotrophic, lactogenic, and gonadotrophic hormones, so that these hormones at least were not concerned in the stimulation of growth, but that it was quite possible that growth in the rat caused by pituitary extract may be due to the synergistic action of other hormones, for example, sex or metabolic hormones.

Laurence-Moon-Biedl Syndrome*Clinical picture*

'Forme fruste.'—R. W. B. Ellis and F. W. Law report a case of infantilism, obesity, and retinal dystrophy in a girl, aged 13, constituting a 'forme fruste' of the Laurence-Moon-Biedl syndrome. In this case the fundus lesions differed from those of typical retinitis pigmentosa in that the pigment disturbances and distribution were atypical, the vessels were not constricted, the disks were not of the pale yellowish colour present in typical cases, and the choroidal vessels are rarely seen in a typical case as clearly as in the authors' case, at least in the early stages. The presence of infantilism and obesity and in members of the immediate family of mental defect and polydactyly, led the authors to include the case in the group of the 'formes frustes' of the syndrome.

Without polydactyly and mental deficiency.—F. D'Abreu and D. Ferriman report what is considered to be a case of the Laurence-Moon-Biedl syndrome without polydactyly or mental deficiency. Before admission to hospital the patient, a woman 25 years of age, had been subject to attacks of tetany about twice a week. The administration of $\frac{1}{2}$ ounce of calcium lactate and 5,000 international units of vitamin D daily greatly lessened the frequency of the attacks.

D'Abreu, F., and Ferriman, D. (1941) *Brit. med. J.*, **1**, 157.

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Evans, H. M., Uyei, N., Bartz, Q. R., and Simpson, M. E. (1938) *Endocrinology*, **22**, 483.

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 Freud, R. I., Levie, L. H., and Kroon, D. B. (1939) *J. Endocrinology*, **1**, 56.
 Li, C. H., Simpson, M. E., and Evans, H. M. (1940) *Endocrinology*, **27**, 803.
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 Meamber, D. L., Fraenkel-Conrat, H. L., Simpson, M. E., and Evans, H. M. (1939) *Science*, **90**, 19.
 Shedlovsky, T. A., Rothen, R. O., Greep, H. B., Van Dyke, H. B., and Chou, B. F. (1940) *Science*, **92**, 188.

PLEURISY

See also B.E.M.P., Vol. IX, p. 699; Cumulative Supplement, Key No. 1277; Surveys and Abstracts 1940, p. 468; and p. 71 of this volume.

Clinical Picture

Radiography in pleural effusions

F. J. Rigos reviews 233 patients with pleural effusions. The age and sex incidence were not of any significance. Pleural effusions are commoner in minimal and moderately advanced pulmonary tuberculosis than in the advanced type. The duration of tuberculosis before the onset of an effusion averaged 13 months and the duration of the effusion averaged 2 months. The effusions were classified according to their X-ray appearances into six groups: (1) 'typical', with the costo-phrenic angle obliterated, diaphragm obliterated, extension of fluid into the axilla; (2) 'massive', with heart and trachea displaced and the diaphragm at a lower level; (3) 'mediastinal', with the mediastinal pleural space filled; (4) 'fluid', with convex level simulating elevated diaphragm; (5) 'fluid', with horizontal level simulating hydropneumothorax; and (6) 'fluid', in interlobar fissure simulating encapsulated effusion. The 'typical' and 'massive' forms were found in 97 per cent of the patients. In the last 4 atypical effusions, a change in the patient's position tends to shift the fluid and assists in diagnosis, especially in the differentiation between large paravertebral abscesses (in cases of tuberculosis of the thoracic spine) and mediastinal pleural effusions. Six predominating types of pulmonary tuberculosis were noted: nodular, fibrotic, cavernous, pneumonic, calcified, and miliary. The nodular and fibrotic forms occurred in 76 per cent of the patients. Cavitation was three times as frequent on the same side as on the opposite side of the effusion. Mortality was higher among patients with a large amount of fluid. The stage of pulmonary disease does not influence the percentage of complete resolution, but it was twice as high in non-aspirated patients than in those aspirated, and in 60 per cent of all cases with complete resolution occurred within 2 years. The presence of fluid also appears to hinder resolution. Obliteration of the costophrenic angle was commonest in cases of incomplete resolution.

Rigos, F. J. (1941) *Radiology*, **36**, 568.

PNEUMONIA, LOBAR

See also B.E.M.P., Vol. IX, p. 713; Cumulative Supplement, Key No. 1279; Surveys and Abstracts 1939, p. 479; 1940, p. 468; and pp. 3 and 71 of this volume.

Course and Prognosis

Mortality and sulphonamide compounds

H. F. Flippin, L. Schwartz, and J. H. Clark, from a review of 800 cases of pneumococcal pneumonia treated with sulphonamide compounds and in which there were 80 deaths, discuss the factors influencing the mortality rate. They found that the mortality rate was 3.5 per cent for patients in the age group 12 to 39, as compared with 15.4 per cent in the higher age groups. With regard to time of treatment, in the entire group 65.3 per cent received treatment during the first 4 days of the disease with a mortality rate of 5.6 per cent; these formed 36.2 per cent of the fatal cases. Whereas patients treated after the fourth day had a mortality rate of 18.4 per cent; these formed 63.8 per cent of the fatal cases. Types I, II, and III pneumococci gave the highest mortality rate (12.2 per cent). Of the fatal cases 40 per cent gave positive blood cultures. In 13 patients in whom serious complications developed, important factors were associated diseases, toxic reactions to chemotherapy and environment.

Examination of sputum

A. W. Frisch states that the microscopical examination of rusty sputum appears to be a relatively quick and simple method of differentiating severe from mild pneumococcal pneumonias. There appears to be a significant correlation between the number of pneumococci per field in the sputum and the incidence of bacteraemia, leucopenia, multiple lobe involvement, and the mortality rate. In a group of 181 patients, prognosis based on sputum counts proved accurate enough to be applicable in individual cases. The number of pneumococci in rusty sputum appears to bear some relation to the number present in some pneumonic areas of the lung. With regard to Type III pneumococcus, however, the number of pneumococci in the sputum does not appear to be closely related to the outcome of the pneumonia.

Treatment

Sulphonamide compounds

Sulphathiazole treatment of infants.—A. V. Stoesser and R. Mooney report on the use of sulphathiazole, the thiazole analogue of sulphapyridine, in 77 cases of pneumonia nearly all

lobar, from January to July 1940 in infants and children. Pneumococcal typing was carried out in 57 cases, a mixed form being found in 6 and a single type in 51, 9 being Type I. The diagnosis of lobar or broncho-pneumonia depended on frequent physical and radiological examinations. The response to the drug was satisfactory; there were not any deaths; and after 48 hours 76 children had a critical fall of temperature. Toxic manifestations were few, the most disturbing being a drop in the polymorphonuclear count; this occurred in 10 cases, but when the drug was discontinued, the leucocyte count at once began to rise. There was little of the nausea and vomiting often caused by sulphapyridine. The incidence of complications was low; there was 1 empyema and 1 abscess of the lung. The results equalled those of sulphapyridine and were better than those of specific serum. Various doses were tried; it was found that 1 grain per pound of body weight was effective, but that $1\frac{1}{2}$ or even 2 grains could be given with safety. The drug should be given every 4 hours, until the temperature has been normal for 3 days. This generally reaches a total of 5 to 6 days of the treatment.

Sulphathiazole.—A contribution to the assessment of the value of sulphathiazole in the treatment of pneumococcal pneumonia is made by I. F. Volini, R. O. Levitt, and H. B. O'Neil, who compared the results in 169 patients treated by sulphathiazole orally and 164 patients treated with sulphapyridine or sulphapyridine combined with immune serum. Dosage of sulphathiazole was as follows: an initial dose of 4 grammes followed every 4 hours day and night by 1 gramme until the temperature remained normal for 48 hours. The blood levels reached in one patient, expressed in milligrams per 100 cubic centimetres of blood were 9 (after 19 hours), 7, 5, 5, 3, 3, 5, 2, 8, and 4. The drug is eliminated from the blood 24 hours after cessation of treatment and from the urine in 24 to 36 hours. The mortality was 5·3 per cent with sulphathiazole (9 deaths, 2 of which were among 24 bacteraemic patients) and 4·2 per cent in the sulphapyridine cases (with 7 deaths, of which 3 were in 25 bacteraemic cases). The toxic reactions resembled those caused by sulphanilamide and sulphapyridine, but the authors consider that the patients are more comfortable on sulphathiazole and that freedom from vomiting and diminished indications for parenteral fluids are worthy of comment. The temperature falls by a combination of crisis and lysis. The authors conclude that sulphathiazole is as effective as sulphapyridine in treatment of pneumococcal pneumonia, and in this series was superior in Types II and VII infection.

C. A. Janeway and P. B. Beeson discuss the treatment of pneumonia and state that sulphathiazole has the advantage over sulphapyridine in that less nausea is caused. In most cases it is not necessary to continue chemotherapy until the time when liberation of antibodies is expected to occur. Relapse is rare if therapy is discontinued after 3 or 4 days. The combined use of chemotherapy with serotherapy is recommended as the most satisfactory form of treatment in severe pneumonia.

W. F. Gaisford and W. Whitelaw employed sulphathiazole in 10 cases of pneumococcal lobar pneumonia. They found that the drug acts similarly to sulphapyridine, though it produces a less rapid fall of temperature. There is also a correspondingly longer period of acute illness. This renders sulphapyridine the more serviceable drug in severe cases of the disease. The chief point in favour of sulphathiazole is that it does not cause vomiting. The authors suggest the possibility that a combination of sulphapyridine and sulphathiazole may prove a valuable routine in the treatment of pneumonia, the first large doses given being sulphapyridine (for example, the first 8 tablets, 4 grammes), and the following ones sulphathiazole. In this way vomiting might be obviated. As an alternative the two drugs could be used together from the onset, for example, 1 gramme of sulphapyridine and 1 gramme of sulphathiazole 4-hourly for the first 3 doses, then 0·5 gramme of each for subsequent doses.

J. P. Scott and A. M. Jones treated 167 cases of pneumonia with sulphathiazole, the dosage being based upon body weight. Of these, 162 patients recovered and 5 died; all the latter were less than 1 year old. Pleuritic effusions occurred in 7 patients; of these, 1 died and was found to have multiple staphylococcal pulmonary abscesses. In 1 case in which sulphathiazole was ineffective, operation was necessary, and Type XXXI antipneumococcus serum was given. In 1 case sulphathiazole was ineffective, and Type VI antipneumococcus serum was used with success; in another case sulphathiazole was ineffective, and sulphapyridine was used with success. In 3 cases sulphathiazole was effective in causing the pleural exudate to resolve. Toxic effects were largely gastro-intestinal, consisting of vomiting and diarrhoea, and were mild in comparison with similar effects caused by sulphapyridine. Sulphathiazole was as effective as sulphapyridine in producing critical falls of temperature in patients with pneumonia. The dosage of sulphathiazole was 1 grain (0·065 gramme) per pound of body weight. The authors conclude that sulphathiazole, employed in moderate dosage for a short time, has proved to be a safe drug, and is easy to administer to young children and infants.

V. B. Callomon and W. E. Goodpastor report on the use of sulphathiazole in 50 cases of pneumococcal pneumonia, with a mortality rate of 8 per cent. The general effect on the temperature curve and clinical course of the disease was similar to that observed with sulphapyridine treatment. Nausea and vomiting were rare, mild and of short duration. The dosage was 4 grammes followed by 1 gramme every 4 hours and the average total dosage was 33 grammes.

Sulphapyridine.—K. G. Kohlstaedt and I. H. Page treated 50 patients with pneumococcal pneumonia with sulphapyridine. Of these patients 3 died. The mortality in patients not receiving specific therapy in the previous 2 years was 48 and 33 per cent. Of the patients

treated with sulphapyridine, 17 were more than 40 years of age; in 23 patients 3 or more days had elapsed since the onset of the diseases, in 8 patients bacteraemia occurred; in 16 patients one lobe, in 29 two lobes, and in 5 three lobes were consolidated. Empyema occurred in 3 patients and sterile effusion in 3. The initial dose of the drug was 2 grammes, followed by 1 gramme at 2 or 3-hourly intervals during the next 36 hours. Subsequent dosage depended on the degree of the toxic manifestations, the rectal temperature at the end of 36 hours, the concentration of free sulphapyridine in the blood, and the change in the number of leucocytes.

Sulphathiazole and sulphapyridine.—C. F. Garvin compares the results obtained by treating 40 patients with typed pneumococcal pneumonia by means of sulphathiazole and 62 patients with sulphapyridine. It was found that approximately twice as much sulphathiazole as sulphapyridine was required to maintain an average concentration of 5 to 6 milligrams of the free drug per 100 cubic centimetres of blood. There was no important difference in mortality between the two groups, the corrected mortality for the sulphathiazole group being 10.3 per cent and for sulphapyridine 8.9 per cent. The administration of sulphapyridine brought the temperature down to normal more rapidly, though a secondary rise was more common than with sulphathiazole. The period spent in hospital was the same in each group. With sulphathiazole vomiting was less common, but there were more crystals in the urine. The initial dose of sulphathiazole was 4 grammes by mouth, repeated in 4 hours, followed by 2 grammes every 4 hours until clinical improvement occurred. Then 1 gramme was given every 4 hours until the temperature was normal for 2 to 3 days and clinical improvement was definite. The average total dose was 53.3 grammes in 5½ days, or 10.1 grammes per day. This dose produced an average level of 5.8 milligrams of free sulphathiazole per 100 cubic centimetres of blood. The initial dose of sulphapyridine was 2 grammes, followed by 1 gramme every 4 hours for 5 doses, and then 1 gramme every 6 hours until the temperature was normal for 2 or 3 days, and clinical improvement was established. The average total dose was 34.4 grammes in 6½ days, or 5.1 grammes per day. This dosage produced an average concentration of 5.4 milligrams of free sulphapyridine per 100 cubic centimetres of blood. With each drug about 3,000 cubic centimetres of fluid was given to each patient daily.

H. F. Flippin, J. G. Reinhold, and L. Schwartz treated 200 adults with typed pneumococcal pneumonia with sulphapyridine, and another 200 with sulphathiazole. The mortality in the two groups was similar. Sulphapyridine appeared to act more rapidly than sulphathiazole as judged by fall in temperature, but the severity and frequency of nausea and vomiting were clearly less with sulphathiazole than with sulphapyridine.

Sodium sulphapyridine intravenously.—C. W. Strickler, Jun., A. P. McGinty, and J. B. Peschau, Jun., employed sodium sulphapyridine intravenously in 54 cases of lobar pneumonia, with a mortality rate of 14.8 per cent. The routine dosage of the drug was 0.06 gramme per kilogram of body weight, in 750 cubic centimetres of physiological saline or 5 per cent dextrose solution. This dose was repeated every 6 hours until the temperature dropped to normal, when similar doses were given every 8 hours. After the temperature had remained normal for 48 hours, the drug was given every 12 hours. It was found that the complications of lobar pneumonia were not prevented by the intravenous injection of sodium sulphapyridine and that toxic reactions were of about the same or of slightly greater frequency than in reported groups receiving the drug orally.

Comparison of effects of hydroxyethylapocupreine and sulphapyridine

W. W. G. MacLachlan, J. M. Johnston, M. M. Bracken, and L. S. Pierce confirm their previous conclusion that comparison of cases of pneumonia treated by (a) hydroxyethylapocupreine and by (b) sulphapyridine show a practically equal mortality. The cases did not include post-operative patients, children under 15 years of age, or patients dying within 24 hours of admission, for little information in treatment is obtained from the moribund. During the 2 years before the report, cases showed a high incidence of *Streptococcus haemolyticus*, associated with the pneumococcus, which should be more favourable for cases treated by sulphapyridine, for hydroxyethylapocupreine has very little, if any, action on the *Streptococcus haemolyticus*. On the other hand sulphapyridine may cause troublesome nausea, vomiting, and even very rarely haematuria, which do not occur when hydroxyethylapocupreine is used in the treatment. A summary is given of the effects for the years 1935–40 of 494 cases of pneumonia treated by hydroxyethylapocupreine; this report showed a marked fall of the total mortality in both the bacteraemic and non-bacteraemic cases. The only evidence of toxicity was occasional and slight nausea and vomiting. There was not any evidence of visual disturbance.

Combined chemotherapy and serum therapy

N. Plummer, J. Liebmman, S. Solomon, W. H. Kammerer, M. Kalkstein, and H. K. Ensworth report the comparative results obtained in 607 cases of pneumococcal pneumonia given by chemotherapy alone and in cases treated by a combination of sulphonamides and serum. The first dose of serum was generally 100,000 units in uncomplicated cases and 200,000 units in bacteraemic cases. This dosage was repeated if necessary. Various sulphonamide drugs were employed. In the drug-alone group the mortality rate was 9.3 per cent, and in the drug-plus-serum group it was 9.8 per cent. In the bacteraemic cases the mortality rate was 28.1 per cent with the drug alone, and 30.0 per cent with drug plus serum. The average response as judged by rapidity of fall in temperature in Type I and Type II cases was not increased by the use of serum. The authors conclude that the present value of serum in

pneumonia appears to be in the treatment of patients who cannot tolerate the sulphonamide drugs, or who do not respond to them satisfactorily within 24 to 48 hours.

Chemotherapy and other methods

In children.—M. Elliott reviews 895 cases of infantile and juvenile pneumonia for the years 1937 to 1939. The important factors in determining the progress were the age of the child, the time of starting treatment, the general condition of the child at the onset, and the type of treatment given. There appeared to be a fall in the mortality rate from atypical pneumonia in the first year of life since the introduction of chemotherapy, but the results of the treatment of lobar pneumonia by chemotherapy alone have been disappointing. Serum plus chemotherapy gave the best results. Children more than 2 years of age should be treated on the same lines as adults. Blood transfusion, parenteral fluids, oxygen, sedatives, and skilled nursing are almost as valuable as chemotherapy in the severe cases of infantile pneumonia.

Preventive

Prophylactic effect of pneumococcus polysaccharide in old age.—P. Kaufman, with the assistance of 5 technical helpers, reports on the active immunization with antigenic capsular polysaccharides during the two years 1937–9 of 1,750 subjects, with 1,870 controls, among the inmates of the New York City Home. Most of the inmates were more than 50, and the great majority between 60 and 80 years of age. The history of the pneumococcal polysaccharides is given, dating from 1897 when A. G. Auld found a specific antigenic substance in the germ-free culture of pneumococci, detailing the large amount of work done, especially at the Rockefeller Institute during this century and including a summary by L. D. Felton, G. M. Ekwurtzel, J. S. Simmons, and L. I. Dublin of mass immunization in west coast camps. In the winter of 1937–8 1,000 inmates of the Home were injected subcutaneously with 0.5 cubic centimetre of a solution containing 1 milligram each of Types I and II polysaccharides; there were 14 cases of pneumonia with 8 deaths; among the 1,120 controls there were 63 cases of pneumonia and 47 deaths. In the year 1938–9 the rate per thousand among the immunized inmates was of pneumonia 12 and of deaths 6.6; the corresponding figures for the controls were 55 of pneumonia and 26.6 of deaths. The conclusions drawn are: (1) though the incidence of pneumonia and the mortality rates in the inoculated subjects seem to be reduced, there is not any appreciable effect on the case fatality rates, (2) the course of pneumonia in the immunized group, as expressed by the length of the attack and the incidence of complications, is apparently uninfluenced, and (3) the prophylactic value is more obvious in the first three-quarters than in the last quarter of the year after immunization.

Cortin and sodium chloride

D. Perla and J. Marmorston showed the value of parenterally administered cortin, in conjunction with sodium chloride and excessive fluid by mouth in severe infections, including 17 cases of pneumonia, in a case of induced malaria with periods of collapse and in severe influenzal infections. Its beneficial effect is shown in the maintenance of blood pressure, decrease in signs of toxicity, avoidance of circulatory collapse, maintenance of appetite and sense of well-being, decrease in the tendency to complications, absence of distention, and shortening of convalescence. The dosage of cortin was 2 to 5 cubic centimetres twice daily intramuscularly or subcutaneously for 2 or 3 weeks. Salt was given by mouth in a dosage of 8 to 10 grammes daily, in 4 divided doses in small amounts of water.

Non-specific treatment

X-ray.—E. B. Settle employed X-ray therapy, unsupported by specific drugs or sera, in the treatment of 34 cases of lobar pneumonia. The mortality rate was 6.2 per cent. X-ray therapy produces a typical clinical reaction in lobar pneumonia, characterized by relief of pain, fall in temperature, dramatic improvement in the patient's general well-being, decrease in leucocytosis, and finally resolution of consolidation.

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POLIOMYELITIS AND POLIOENCEPHALITIS

See also B.E.M.P., Vol. X, p. 12; Cumulative Supplement, Key No. 1282; Surveys and Abstracts 1939, pp. 42 and 484; 1940, p. 476; and p. 49 of this volume.

Aetiology

Toxic factor in stools

J. A. Toomey and W. S. Takacs report experiments on the extraction of a toxic factor from stools of patients with poliomyelitis. This was shown, by the injection of stool emulsions into guinea-pigs, to accelerate the production of poliomyelitis and to remain toxic for at least six generations. Filtration removed the factor but the sterile eluate was as toxic as the whole stool emulsion. It was not found to be present in extracts of brain and spinal cord. It is known that convalescent patients with poliomyelitis show a rise in the agglutinin titre of their blood serum against enteric organisms. The authors showed by experiment that serum from convalescent patients had a neutralizing effect upon the action of the toxic factor as well as on the poliomyelitic virus itself. The factor may be due to the increase of virulence of intestinal bacteria or to a combination of stasis and the virus itself.

Tonsillectomy

A. E. Fischer, M. Stillerman, and H. H. Marks report that, among children between the ages of 3 and 12 years, in the Toronto epidemic of 1937, acute poliomyelitis developed more often in those who had recently undergone tonsillectomy than in others. Among the children with poliomyelitis, the incidence of the bulbar form was more than twice as high in those whose tonsils had been removed at any time previously, as in those with tonsils intact.

Immunity and Resistance

Formation of antibodies

Olfactory mucosa.—R. H. Allen and P. F. Clark, investigating the olfactory mucosa as a possible source of anti-poliomyelitic substances, found indications that certain of the protein fractions possess weakly neutralizing properties. The soluble components of the olfactory mucosa of a naturally resistant animal (the calf) failed to neutralize the poliomyelitis virus consistently.

Epidemiology

Field of contagion in children

M. Bashford, in a comprehensive review of acute poliomyelitis, notes the recent increase in its prevalence which, however, is low as compared with other epidemic diseases. Although the distribution is world-wide, severe epidemics generally occur in temperate regions only. The high incidence in late summer and autumn cannot be explained, although association with temperature change, transmission by ripening fruit, and seasonal bodily changes have been suggested. There was formerly a higher rural, than an urban, incidence, but now the latter is more even. There is not any definite periodicity, but there appears to be an infection-free period following an epidemic, with a tendency to revisitation of the same area. Although maximum susceptibility is generally found in children of 2-3 years of age, a tendency to attack older children has recently been observed. A survey of three epidemics on adjacent islands even showed immunity among children. The immunity of children under 1 year can be partially attributed to the persistence of maternal antibodies. There is little evidence for racial immunity. The greater immunity of females and of individuals of the B agglutinin (only) blood group is noted. Observations on bodily features of those infected suggest some relationship, but conclusive evidence is lacking. The virus is considered to be specific and filtrable and of several strains with immunological differences. Evidence points to the olfactory nerve as the path of entry of the infection, although entry as a result of tonsillectomy is possible and produces bulbar infection via the peripheral nerves. There is good evidence of transmission by carriers and a strong suggestion that they may be the sole transmitters; water, milk, and sewage may be factors, although there is doubt as to their significance. The incubation period is difficult to determine, but is usually 7-10 days, during which time the person may be infective. The first attack gives complete immunity which can be acquired by serum injections from immune or convalescent individuals. There are two hypotheses of immunity: (1) the subclinical which advocates immunity due to exposure only to virus, and (2) the maturation hypothesis, advocating the growth of general immunity with maturity.

Treatment

The infection

Sulphapyridine and anti-serum.—S. Miller and S. Wray employed sulphapyridine either alone or combined with convalescent poliomyelitis serum during an outbreak of poliomyelitis of moderate severity. The initial dose of sulphapyridine by mouth was 2 grammes and 1 gramme

was repeated every 4 hours until the temperature settled, unless there were serious contraindications. Twenty cubic centimetres of convalescent serum were given intramuscularly and in some cases this dose was repeated once or twice. Patients with more acute symptoms, in which paralysis was impending or had already developed, were given 2 or 3 grammes of sulphapyridine soluble in physiological saline intravenously together with 20 cubic centimetres of convalescent serum intramuscularly. The drug was repeated every 4 hours until 8–10 grammes had been given. A second dose of 20 cubic centimetres of the serum was given 8 to 10 hours after the first. Next day the drug and the serum were repeated.

Serum injections.—M. S. Duran reports a new method of treating acute poliomyelitis based on the specific direct antibody production. From 8 to 12 cubic centimetres of the patient's spinal fluid are injected into the ear vein of a rabbit. The next day 14 cubic centimetres of the rabbit's blood are withdrawn from the heart, centrifuged, and injected intramuscularly into the patient's buttock. Next day another 14 cubic centimetres of the rabbit's serum are injected and the following day another rabbit is treated in the same manner, and next day 12 cubic centimetres of its blood withdrawn and injected into the patient. The author claims remarkable results from this treatment.

Potassium chlorate.—S. O. Levinson and A. Milzer report on the use of potassium chlorate in the treatment of experimental poliomyelitis. Thirteen rhesus monkeys were inoculated intracerebrally with the virus of the disease. Potassium chlorate therapy was begun, in 7 monkeys, 4 hours after inoculation of the virus, and this medication was continued for 9 days. The remaining 6 animals served as controls. There was no indication that the treatment had any therapeutic value. In neither group did any animal escape the disease: severe paralysis appeared in as many in one group as in the other; the incubation period was identical, as were the pathological changes and the degree of neurone destruction.

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PREGNANCY: NORMAL AND PATHOLOGICAL

See also B.E.M.P., Vol. X, p. 48; Cumulative Supplement, Key Nos. 1291–1303; Surveys and Abstracts 1939, pp. 29 and 488; 1940, pp. 17 and 477; and p. 16 of this volume.

Physiology

Hormones in pregnancy

Excretion of pregnanediol after removal of ovarian tissue.—G. E. Seeger and E. Delfs report on the pregnanediol excretion throughout pregnancy in a woman from whom all ovarian tissue had been removed on the sixty-third day of gestation. She did not show any abnormality during pregnancy and parturition, but the pregnanediol excretion never rose above the level generally present during the first 90 days, for example, values comparable with those found during the luteal phase of non-pregnancy cyclic women. The authors consider that this strongly supports the view that the corpus luteum hormone has an extra-ovarian source during the last two-thirds of gestation by the fact that the patient continued to excrete pregnanediol in the urine during the last 7 months of pregnancy after the removal of all ovarian tissue. The placenta seems to be the most probable source of the pregnanediol, although a different origin might be argued in these circumstances, as D. Beall and T. Reichstein have isolated progesterone and allopregnanolone from adrenal extracts.

Pregnancy toxæmias and nephrosclerosis

Experimental findings.—L. V. Dill, C. E. Isenhour, J. F. Cadden, and A. Kuder found that repeated pregnancies in rabbits with varying degrees of hypertension produced by renal ischaemia had not any apparent effect on blood pressure, albuminuria, or histological renal changes. The expectation of life in these animals appeared to be decreased. In a large percentage of the animals foetal resorption and death occurred. The authors consider that there is evidence of a common aetiological agent of pregnancy toxæmias and the nephroscleroses.

Diagnosis of Pregnancy

Antuitrin-S skin test

T. E. Mandy and A. J. Mandy report on the antuitrin-S skin test in 523 cases of presumed early pregnancy. Of the pregnant subjects, 93 per cent were diagnosed correctly and 7 per cent incorrectly. Of the non-pregnant women, 72 per cent were diagnosed correctly and 28 per cent incorrectly. The authors conclude that this test is not an adequate substitute for Friedman's or the Aschheim-Zondek tests.

Urinary excretion of pregnanediol

C. L. Cope states that pregnanediol is a product of corpus luteum and placental metabolism. Its excretion in the urine is relatively easily measured in any biochemical laboratory. The author attempted to assess the diagnostic value of pregnanediol excretion in abnormal pregnancy. Its complete absence is nearly always evidence of serious abnormality, suggesting in

early pregnancy the imminence of abortion, and in late pregnancy the death of the foetus. The significance of a low pregnanediol excretion still remains uncertain. A normal pregnanediol excretion is not evidence that abortion will not occur or that the foetus is still alive. Chronic nephritis and toxæmia of pregnancy may interfere with pregnanediol excretion. In these conditions deviations from the normal excretion do not necessarily mean that pregnancy is abnormal.

C. L. Buxton states that pregnanediol is an excretion product of the corpus luteum hormone progesterone. Its synthesis as sodium pregnanediol glycuronide probably occurs in the liver. Its metabolism and excretion do not depend upon the uterus or ovaries. The greatest yield and purest form of pregnanediol glycuronide occurs in the urine of pregnancy. No pregnant women have been observed who do not excrete this substance. The negative diagnosis of pregnancy may therefore be made as a result of negative pregnanediol determination. Pregnanediol is present in small amounts in the urine during the latter half of the menstrual cycle in normal women. It was apparent that pregnanediol is excreted only during the time that the endometrium is being activated to a secretory phase.

The xenopus test

A. I. Weisman and C. W. Coates find that commercial extracts of anterior pituitary-like hormone from pregnancy urine, when injected into the female *Xenopus laevis*, can induce ovulation and extrusion of hundreds of ova from the South African clawed toad within 18 hours. The anterior pituitary-like hormone of pregnancy urine is the responsible factor in the xenopus test for the diagnosis of pregnancy. Amounts of the hormone in excess of 50 rat units are required to produce the reaction. It is hardly likely that such large amounts of the hormone could be found in normal urines in the quantities injected into the xenopus.

Friedman test

Positive results in non-pregnant states.—E. P. McCullagh and W. K. Cuyler found positive Friedman tests in 241 out of 2,134 cases in which neither pregnancy nor any evidence of chorionic tissue was present. In 1,774 tests in women, 172 gave positive reactions, and of 360 tests in men, 69 gave positive reactions. Among the conditions other than pregnancy in which the Friedman test may be positive are psychoses, hysteria, epilepsy, and arterial hypertension in the absence of gonadal failure. Often it is positive about the time of puberty, and in primary disease of the pituitary, such as acromegaly or tumour, and also in organic lesions of the hypothalamus. Positive tests may be present in cases of dwarfism, in some cases of obesity, in hypothyroidism, diabetes mellitus, adrenal cortical hyperfunction, alopecia areata, progressive myopia, keratoconus, and functional ovarian deficiency. The test is useful in determining whether or not there is an abnormally large excretion of gonadotrophic hormone in non-pregnant states.

Haemorrhages

Fatal adrenal haemorrhage in an adult

R. A. MacKenzie records a case in a multipara, aged 35, in the thirty-sixth week of her fourth pregnancy, who was attacked by very severe abdominal pain, especially in the right costovertebral region and became gravely collapsed. This was followed by labour and delivery of a still-born male. Death occurred 42 hours after the onset of pain. Necropsy showed pneumonia of the lower lobe of the right lung, calculi and hydronephrosis on the right side and bilateral pyelonephritis, and haemorrhage into both adrenals, to which death was ascribed.

Hyperemesis Gravidarum

Aetiology

J. W. Finch states that the nausea and vomiting of pregnancy develop at the same time as the corpus luteum reaches an appreciable size. The symptoms disappear at about the time the gland is known to begin to undergo retrogressive changes. In 98 patients with nausea and vomiting of pregnancy, a cutaneous reaction directly proportional to the degree of the severity of the symptoms occurred when injected intradermally with from 0.02 to 0.03 cubic centimetre of progestin (natural) in oil. A control series of patients who were not nauseated and in the pregnant state gave negative cutaneous reactions to intradermal progestin. Of 51 patients treated with progestin in oil along the lines of allergic desensitization, 91.2 per cent were relieved of their symptoms. A control series of patients treated and skin-tested with synthetic progesterone in oil failed to react or to be relieved of their symptoms. A high percentage of the patients with nausea and vomiting of pregnancy either had other diseases of allergy or gave a family history of allergy. The author concludes that the nausea and vomiting of pregnancy are due to an allergic reaction of the patient to the secretion of her own corpus luteum. The luteal hormone acting as an allergen is not progesterone, but is an unidentified hormone of the corpus luteum. Desensitization may be accomplished by injection of graduated doses of progestin in oil.

Toxaemias of Late Pregnancy

Treatment of eclampsia

Veratrum viride therapy.—R. D. Bryant and J. G. Fleming, employing hypodermic injections of veratrum viride (green hellebore) in conjunction with other measures in 120 consecutive cases of eclampsia, obtained the low gross mortality rate of 1.67 per cent. The drug has apparently a vasodilator action and, in the presence of eclampsia, acts by relieving wide-

spread vasoconstriction. Dilatation of the arterioles causes a more normal blood supply to become available to the tissues, and various therapeutic agents, such as magnesium sulphate, have a more ready access to them. There is also a decline in blood pressure. Recovery from the acute stage is the criterion for determining when induction of labour should be attempted, and the simplest methods of induction were tried first. In the 43 cases of ante-partum eclampsia requiring induction of labour the average interval between apparent control of convulsions and the first attempt to induce labour was almost 58 hours. In no case did treatment fail, and there were no deaths from eclampsia or any of its immediate complications; the 2 deaths which did occur were from sepsis and occurred on the fourteenth and the sixty-fifth day respectively post-partum. Treatment was as follows: Ten minims (0.6 cubic centimetre) of a veratrum viride preparation, the nature of which is not stated, are given hypodermically at once, and repeated every 10 to 15 minutes until the pulse rate is below 60 or the systolic blood pressure is below 120 millimetres of mercury. Thereafter, until the patient is conscious, the preparation is repeated in 3 to 10 minim doses, if the pulse rate rises above 80 or the blood pressure above 150. After the patient becomes conscious and cooperative, 3 to 10 minim doses are given if the patient is nauseated or has severe headache, marked visual disturbances, epigastric pain, or convulsions. Ten cubic centimetres of 50 per cent magnesium sulphate solution are given by deep injection at once, followed by 5 cubic centimetres every 6 hours for 4 doses, and then 5 cubic centimetres every 12 hours for 4 doses. Five hundred cubic centimetres of 20 per cent dextrose are given intravenously at once, and repeated every 6 to 10 hours until consciousness returns. A catheter is passed and a soapsuds enema given. Fluids (5,000 cubic centimetres daily) by mouth are forced as soon as possible. No sedatives are given, except for extreme restlessness or labour. A salt-free diet is given as soon as it is tolerated. The fluid intake and urinary output are measured, and the urine examined daily for albumin.

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PROSTATE DISEASES

See also B.E.M.P., Vol. X, p. 146; and Surveys and Abstracts 1939, pp. 158 and 493; 1940, p. 482.

Prostatitis

Treatment

Staphylococcus toxoid.—A. C. Drummond treated with staphylococcus toxoid 27 cases of prostatitis, in which the staphylococcus was either the only, or the predominant, organism. The initial intradermal skin dose of the toxoid was 0.01 cubic centimetre, injected into the volar aspect of the forearm. If the resulting erythema, in 24 hours, was 3 by 3 inches or less, a bi-weekly subcutaneous injection of 0.1 cubic centimetre of the toxoid was given, with doses increasing by 0.1 cubic centimetre in alternate deltoid regions. When 1 cubic centimetre was reached the dose was repeated weekly for 2 months. Prostatic massage was done every 10 days to promote adequate drainage. In 25 of the 27 cases there resulted relief of initial symptoms, subsidence of initial signs, generalized constitutional improvement, final negative prostatic smears, absence of staphylococci from the culture of the prostatic fluid, and satisfactory removal of all infective foci.

Tuberculosis

Aetiology and clinical picture

The rare condition of isolated tuberculosis in the prostate is illustrated by a case described by G. W. Strom and G. J. Thompson. The patient, aged 30, had abdominal pains which had previously been accompanied by jaundice, acholic stools, and dark urine. There was a previous history of bronchial asthma due to pollen sensitivity. There were not any specific genital symptoms. X-rays and the von Pirquet's tuberculin test, together with a physical examination, did not show any signs of tuberculosis or abnormalities in any organs. After a difficult operation for subacute cholecystitis with multiple gall-stones, the patient died. Necropsy brought to light a purulent abscess of the prostate containing tubercle bacilli and a typical tuberculous structure. No tuberculosis was found in the genital or other organs. It has been commonly believed that the epididymis is always the primary site of tuberculosis of the genital organs. No conclusion is drawn as to the mode of entry.

Simple Enlargement

Clinical picture

Largest recorded prostate.—O. A. Nelson reports the case of a man, aged 89, from whom the prostate, which weighed 720 grammes, was removed by morcellment. After removal of this, the largest recorded prostate, the bladder was found to be practically within the abdomen. Histologically the prostate did not show any evidence of malignancy, although there was a carcinoma of the bladder.

Incidence.—G. J. McHefsey, on the basis of histological examination of tissue removed from the prostate by transurethral resection, in 300 cases, found that the incidence of carcinoma for men of all ages is 11·7 per cent. On the basis of 50 cases in which the clinical diagnosis was carcinoma of the prostate, the urologists made a correct or partly correct diagnosis in 88 per cent of the cases. In 150 cases in which the clinical diagnosis was benign hypertrophy of the prostate, the diagnosis was correct in 96 per cent of the cases. In 50 cases in which the pathological diagnosis was adenofibromatous hyperplasia, the surgical pathologists were correct in 98 per cent of the cases.

Differential diagnosis

Importance of intravenous pyelography.—In a practical article under this heading C. Morson points out that there is a tendency, particularly among the laity, but sometimes also among medical practitioners, to ascribe any alteration in micturition in old men to prostatic disease. Although increased frequency of nocturnal micturition is commonly the first sign of prostatic obstruction, it is equally evidence of diabetes and chronic interstitial nephritis. These conditions should be excluded before any further investigation, and especially before the passage of a catheter. Complete examination of the urinary tract is essential for accurate diagnosis, but must be carried out with the greatest care, especially in patients who have not previously undergone urethral instrumentation, for there is much variation in the tolerance of the urethra. Intolerance may be shown by spasm of the compressor urethrae, by shock, or, if there is a chronic infection of the bladder, seminal vesicles, or prostate, by an acute infection. One out of five men has prostatic adenoma and it is therefore important to decide if this, rather than chronic renal disease, is responsible for the symptoms. If both these lesions are present, to which should attention be directed? If symptoms other than increased frequency due to prostatic disease, such as residual urine of 1 ounce or more, can be excluded, a diagnosis of renal disease is justified. Every old man with prostatic disease has albuminuria and a raised blood-urea. More important than laboratory tests is intravenous pyelography, which shows changes in the urinary tract due to back pressure caused by prostatic obstruction. Prostatic disease and colon bacilluria resemble each other in many respects—haematuria, frequent and difficult micturition, and retention, and bacilluria may complicate prostatic enlargement. The answer to the question often asked by patients, 'As I have difficulty in passing water and I am told it is due to enlargement of the prostate, how can I avoid an operation?' is simple: the patient should be reassured by telling him that the disease is not necessarily progressive and that by an annual medical examination it may be possible to control threatened complications. He should at once satisfy the urge to micturate, otherwise retention may be precipitated. When a septuagenarian approaching eighty suffers from symptoms of simple prostatic enlargement so urgent as to demand instrumental interference, no major operation is justifiable unless he refuses to submit to the minor surgical procedure of permanent cystotomy, or catheterization.

Diagnosis

X-rays.—E. L. Peirson and S. A. Wilson describe a new X-ray method of estimating the size of the prostate gland. Its advantage over cystoscopy is that it obviates injury of the prostatic urethra. By its use it is possible to estimate the amount of tissue which must be removed, and thus to determine the most satisfactory type of operation. The method depends primarily on observing by means of X-rays the position of the balloon of a Foley catheter which has been placed in the bladder.

Treatment

Testosterone propionate.—C. D. Creevy and C. E. Rea state that the aetiology of benign hypertrophy of the prostate remains uncertain. They treated 23 cases of mild to moderate benign hypertrophy with testosterone propionate. Sixteen were benefited, 5 were not affected, and 2 grew worse. Five of the improved patients returned with recurrent symptoms; it was found that the injection of inert substances had the same effect as that of the testosterone propionate had previously produced. The authors conclude that it remains to be demonstrated that the injection of testosterone propionate in cases of benign prostatic hypertrophy is more than a form of psychotherapy.

M. J. Markham found that in 7 cases of benign prostatic hypertrophy the use of testosterone propionate gave moderate and marked relief of all the symptoms of prostatism. The treatment consisted of the intramuscular injection of 25 milligrams of the drug 3 times a week for 3 weeks; after this the patients were given 10 milligrams of the drug 3 times weekly for a further 3 weeks. In many cases nocturnal enuresis and dysuria completely disappeared. The author considers that testosterone propionate is indicated for the symptomatic treatment of benign hypertrophy of the prostate in cases in which operation involves a clear risk to the patient's life, when the palliative operation of trans-urethral prostatectomy has been unsuccessful,

and in mild cases in which surgery is not urgent and the patient is unwilling to submit to any form of surgical treatment.

Malignant Disease

Carcinoma

Direct extension to ureter.—W. H. Higgins reports a case of carcinoma of the prostate, in a man aged 64, with an unusual ureteral extension. Serial sections of the tissues around the prostate, seminal vesicles, and ureter showed the process is one of direct extension and not of metastasis. From a review of the reported cases, it appears that there are only 23 cases on record of ureteral metastases, and of these 8 were from primary carcinoma of the prostate and 3 from primary carcinoma of the cervix or bladder.

Calculi

Treatment

Trans-urethral removal.—J. L. Emmett discusses the suitable treatment of prostatic calculi and points out that, contrary to general opinion, in very few cases of prostatic calculi are the stones too large to be removed or crushed trans-urethrally. If too large to be removed through the cystoscope they can be manoeuvred into the bladder to be crushed by a lithotrite. In very extensive calculous replacement of the prostate, a few calculi may be left after trans-urethral operation, and usually do not cause any further trouble. Most prostatic calculi do not cause symptoms and therefore are not important. The symptoms, when they do occur, are frequency, burning pain on micturition, and urgency of urination, an inadequate urinary stream, haematuria, and partial or complete urinary retention. The author's practice is illustrated by the treatment of a man, aged 73, with paralysis agitans, diabetes mellitus, arteriosclerosis, extreme senility, and periods of disorientation. The prostate was enlarged, hard, and suggested carcinoma; the blood pressure was 180 systolic and 120 diastolic millimetres of mercury. Radiologically the place of the prostate was almost entirely taken by multiple large calculi. The McCarthy panendoscope was introduced into the urethra and showed several large ducts on the floor of the prostatic urethra. A Collings knife, inserted through the panendoscope, incised the ducts, and exposed several large cavities filled with prostatic calculi, some measuring as much as 3 centimetres in diameter, and occupying the whole of the prostate. The calculi were dislodged one by one into the bladder, and the panendoscope withdrawn; Bigelow's lithotrite was then introduced and litholapaxy carried out with success, the former symptoms disappearing completely.

Creevy, C. D., and Rea, C. E. (1940) *Urol. cutan. Rev.*, **44**, 430.

Drummond, A. C. (1941) *Amer. J. Surg.*, **51**, 393.

Emmett, J. L. (1941) *Proc. Mayo Clin.*, **16**, 289.

Higgins, W. H. (1941) *Johns Hopk. Hosp. Bull.*, **68**, 337.

McHefey, G. J., (1940) *Proc. Mayo Clin.* **15**, 458.

Markham, M. J. (1941) *Urol. cutan. Rev.*, **45**, 35.

Morson, C. (1940) *Practitioner*, **145**, 9.

Nelson, O. A. (1940) *Urol. cutan. Rev.*, **44**, 454.

Peirson, E. L., and Wilson, S. A. (1941) *J. Urol.*, **45**, 82.

Strom, G. W., and Thompson, G. J. (1941) *J. Urol.*, **45**, 858.

PRURITUS AND PRURIGO (HEBRA)

See also B.E.M.P., Vol. X, p. 165; and Surveys and Abstracts 1939, p. 496.

Prurigo (Hebra)

Clinical picture

Unusual type.—J. H. T. Davies reports 2 cases of an unusual eruption which he calls prurigo annularis. It consisted of an expanding ring, the periphery of which had the form of an ill-defined band, 1 to 2 inches wide, of minute urticarial or acuminate papules, 25 or so to the square inch; the more central of these had had their tops scratched off. This enclosed a uniformly pigmented refractory area. The eruption tended to appear, or to be aggravated, during pregnancy.

Davies, J. H. T. (1941) *Brit. J. Derm.*, **53**, 143.

PSITTACOSIS

See also B.E.M.P., Vol. X, p. 175; Cumulative Supplement, Key No. 1311; and Surveys and Abstracts 1939, p. 496; 1940, p. 484.

Treatment

Sulphapyridine

H. C. Hinshaw reports 2 clinical cases of psittacosis. One patient had pneumonia in the lower part of the right lung with a temperature of 104.6° F., and accordingly was given 2 grammes of sulphapyridine by the mouth for 2 doses at 4-hourly intervals, and then 1 gramme every 4 hours for 8 additional doses. Within 24 hours the temperature fell to normal and the pulmonary signs and symptoms diminished. This treatment was then abandoned because of a history of renal disease, and of recent vomiting, hiccup, and slight elevation of the blood-urea, and was not resumed, although the patient's temperature slowly rose to 101.8° F. In the other patient chemotherapy was not employed as the diagnosis was not established until

inexplicable vagaries in the clinical syndrome of disorder. The definition of the conscious mind is not the concern of the physiologist, who is interested only in the relation between conscious and reflex behaviour and the levels at which physiological consciousness appears. The distinction between functional and 'organic' disorders, between mental and physical disorders, are not wholly valid, as all cerebral activity has a physical basis, and a physiological approach to inhibitions, for example, can often be more effective than the tortuous approach of the psychologist. There is occasionally even a gross anatomical defect causing abnormal behaviour. Thalamic syndrome, causalgia, and the phantom limb phenomenon emphasize the unity of psychological and physiological phenomena. The first alone has definite substance, but all three are clearly the outcome of central nervous disorder. Similarly, persistent fear can be regarded as prolonged over-reaction to an excessive stimulus. The distinction between normal reaction to a stimulus and affective disorder is often arbitrary and based on the time taken for recovery. The distinction also between psychoses and neuroses in affective disorders is no more than quantitative and based on the extent to which a person is involved in the disorder; for example, a patient might be psychotic during one part of the day and merely neurotic for the rest of the 24 hours. Mild or partial disorders (neuroses) are generally characterized by general or specific fears, by general malaise and fatigue which may nevertheless be as real as the thalamic syndrome and result from central nervous disturbance. In more severe disorders (psychoses), hallucinations are common, visceral disturbances without any functional disorders, loss of various emotions all corresponding with the neurological conception of disorder at the level of feeling tone. In addition there are actual physiological disorders of certain functions. Preoccupations associated with depressions are common, but to attempt to decide which is the cause and which the effect, for example, whether sadness is the outcome of sad thoughts or vice versa, is again to make an artificial distinction between externally stimulated neurosis and inherent psychosis. There is no known cause of affective disorders, and precipitating causes are varied and difficult to detect. The passage of time may possibly precipitate slowly accumulating disorders and conversely precipitate recovery, and so-called psychotherapeutical cures may often be due to routine treatment and long rest. What psychiatry can do is to adjust the patient to a better technique of living by management, medical and even surgical treatment, and sometimes, as in convulsant therapy, effect a cure. Without belittling the value of the Freudian approach to hysteria and neurosis, it tends to exaggerate the 'evasive' and 'gain' motive in affective neurosis and to assume that the latter will disappear when the patient is conscious of the motive, which is certainly true in many, but not in all cases. The claim that medical psychology alone can deal with the treatment of neuroses and that the psychiatrist should confine his attention to the psychoses is again based on a false distinction between these categories. Furthermore, many problems of medical psychology cannot be solved without knowledge of neurology. The success of medical psychology had so far been based on the fine personalities of the leading figures. This is the important factor and not an elaborate technique. The drawing together of the neurologist and the psychiatrist on the understanding that the brain is the organ of mind is desirable and inevitable, and upon this depends how long psychology remains a separate branch of medicine.

Reactions to traumatic experiences

Influence of war on mental disease.—R. E. Hemphill publishes a study of the effect of war on mental disease, largely based on an analysis of the experience of the Mental Hospital at Bristol, a town which has gone through many air-raids and other disturbing factors. It was generally anticipated that war would exert a shattering effect on the mental health of the civil population. The number of patients admitted to the Bristol Mental Hospital in 1940 was the lowest in 5 successive years, and exactly 100 less than in 1938. After careful examination of the histories of all patients it was only possible to find 17 men and 14 women, or 31 out of 354 admissions, in whose illness war seemed to have played any part, family or constitutional taints being present in most of these cases. The ratio of patients discharged 'recovered' to cases admitted in 1940 (33 per cent) is exceeded in 3 only of the last 10 years. As regards the reactions of patients in the mental hospital it appears that on the whole the protective shield of psychotic illnesses effectively damps out the realities of war. It is as if the patients were observing an action which had no greater reality than the action on the screen of a cinema. The chronic non-deteriorated individual probably regarded as a psychopathic personality was the exception. In conclusion it may be said that up to the present time, whatever may happen later, the war has had little adverse effect on the mental health of the general population and has been of benefit to some types of individuals, especially women. Other publications to the same effect are quoted.

Civilian reactions to air-raids.—F. Brown classifies civilian psychiatric air-raid casualties into three groups: (1) mild and severe emotional shock, treated by rest and sedation, rehabilitation, occupational therapy, or transfer to congenial surroundings; (2) psychoneurosis, generally hysteria, associated with amnesia for the provoking incident. These patients should be treated by psychotherapy or by evipan narcosis, designed to eliminate the hysterical amnesia, and by occupational therapy; (3) psychoses, generally panic and depressive states. Personal insecurity is present in most patients who acquire a psychosis after bombing. They are treated in the same ways as are the corresponding psychoses of peace-time.

Hysterical paralysis in a soldier.—J. Rickman reports on the case of a soldier, aged 28, who, after normal recovery from superficial wounds, was affected by hysterical paralysis of the

arm on returning from sick leave. Psycho-pathologists in the period of the war of 1914-18 would have laid emphasis on the fact that the patient had wandered to the coast during a retreat and would have attributed the paralysis to a conflict between the instincts of self-preservation and social responsibility. At the present day emphasis is laid on objective personal relationships, and the most significant facts were thought to be the death of a companion in battle and a close link in the patient's mind between this friend and the arm. Attempts were made to link up these thought associations in the conscious mind of the patient, who later began to take renewed interest in military drill and made progress.

Obsessive-compulsion neuroses

Leptazol therapy.—M. Zeifert reports on a case of severe compulsion neurosis in a man aged 51. The family history showed neurotic tendencies and the personal history revealed progressive symptoms of neurosis throughout life. The main symptom was anxiety over trivial matters, particularly about obtaining food. There was an obsessional anxiety to memorize unimportant facts and numbers, and a terror of not being able to retain them. The author attributes this to anal eroticism, shown in the retention of faeces during childhood. Much of the general anxiety was attributable to sexual frustration; it diminished with a more satisfying sex life, increasing again on abandoning this life. There was a strong sense of guilt and an obsessional compulsion to perform trivial actions. Although the neurotic symptoms became more prominent at the age of 22, there was not any single precipitating cause. The author diagnoses the case as one of severe compulsion neurosis. Four years of treatment in mental hospitals and institutes failed to bring about any improvement. The patient was cured by leptazol (cardiazol) convulsions. Three sub-convulsive doses had no effect, but 16 *grand mal* doses (from 4 cubic centimetres up to 7 cubic centimetres of 10 per cent leptazol) progressively cured him. The explanation of this cure is lacking.

Psychotherapy

General treatment

Satisfactory results in elderly patients.—G. W. Robinson, Jun. states that the results to be expected from psychotherapy in old people are as good as those in younger patients with mental disorders. In 50 patients over 60 years of age with abnormal mental reactions, pathological changes of a destructive or deteriorative character were solely responsible in only 14 (28 per cent). Thirty-six, or 72 per cent, were the subject of mental illness that responded to modern treatment, and 33, or 91·6 per cent, of these recovered sufficiently to go home in an average time of 6 weeks of treatment. Of 20 such patients with whom the author was able to maintain contact, 17, or 85 per cent, remained well at the end of 6 months.

Brown, F. (1941) *Lancet*, **1**, 686.

Hemphill, R. E. (1941) *J. ment. Sci.*, **87**, 170.

Rickman, J. (1941) *Lancet*, **1**, 785.

Robinson, G. W., Jun. (1941) *J. Amer. med. Ass.*, **116**, 2139.

Symonds, C. P. (1941) *Proc. R. Soc. Med.*, **34**, 289.

Zeifert, M. (1940) *J. nerv. ment. Dis.*, **92**, 290.

PSYCHOSES: AFFECTIVE PSYCHOSES

See also B.E.M.P., Vol. X, p. 267; Cumulative Supplement, Key No. 1319; Surveys and Abstracts 1939, pp. 118 and 498; 1940, p. 487; and p. 79 of this volume.

Aetiology

Role of sex hormones in psychiatry

M. Reiss contributes a critical review of the evidence, much of which is nebulous, of the part played by gonadotrophic hormones in mental disorders. This article is accompanied by 157 references, and attention is directed to four main questions. (1) What variations of brain function are due to disturbance in the production of sex hormones? Here the effects of castration and of the climacteric, including the climacterium virile (K. Mendel, 1910), are described separately in the two sexes. In male hypogonadism the psychical changes after castration are not the immediate psycho-pathological result of hypogonadism, but the final product of a chain of many progressively developed symptoms. In this section the mental manifestations in connexion with sex life are discussed, those with an ill-balanced mentality being more prone to succumb to various depressions. In the female, hypogonadism, whether due to castration or climacteric, is very much alike, differing if at all only on its more or less rapid development; the metabolic changes include alteration in the distribution of excessive fat, and not in the body as a whole. As the so-called sex hormones are not produced in the gonads exclusively, it is pointed out that it would be better to speak of an increased production of these hormones rather than of hypogonadism. This occurs at puberty, and the author does not rule out the possibility that masturbation may cause disturbance in hormone production with secondary psychological dysfunction. (2) What variations in the production of sex hormones can be noted in some disturbances of cerebral function? Symptoms of endocrine disorders are present in a large number of psychotic patients—it is said in half to three-quarters of the inmates of mental hospitals—but it is important to remember that disturbance of sex hormone production alone is seldom present, and is commonly combined with disorder of the thyroid or adrenal cortex. As pointed out by F. W. Mott (1921), there is a close relation between schizophrenia and morbid changes in the gonads, but it is still uncertain

which is primary. (3) How far can experiments concerning the instinctive behaviour and the physiological reactions of animals under the influence of sex hormones, assist in the analysis of the pathogenesis of some cerebral disorders? This contains a useful summary of the results obtained by about 40 workers. (4) Are disturbances in the endocrine production of sex hormones ever a primary cause of mental disease? Examples of this relation are given but it is pointed out that at best gonadal dysfunction can only initiate the first stage of a mental disorder—whether climacteric or schizophrenic or other change of brain function.

Treatment

Sub-convulsant therapy

G. C. Young describes the use of leptazol (synonyms—cardiazol, metrazol, phrenazol) in sub-convulsant doses in a woman of 38 who was admitted to hospital in an acutely confused, destructive, and restless state with vivid auditory and visual hallucinations. She was given 5 cubic centimetres of a 10 per cent leptazol solution intravenously, and 6 cubic centimetres one minute later. There was little reaction, and no convulsion. Next morning 6 cubic centimetres and 7 cubic centimetres were given, and in the evening 7 cubic centimetres and 8 cubic centimetres without convulsion. Mental improvement was already apparent. A few days later 4 cubic centimetres were given without convulsion, but with further mental improvement. Three weeks later treatment was discontinued and the patient made a full recovery.

Non-convulsant therapy.—G. Caplan reports the results of the non-convulsant faradic shock therapy in a case of acute mania in a man aged 30. This patient, who had not responded to other forms of non-convulsive therapy, was brought to normal in 6 days. With increasing normality there occurred a strange increase in sensitivity to the faradic current, and finally a major convulsion, with all its dangers, was produced by a current three-quarters of the normal strength—a current which other patients can tolerate with equanimity.

Involucional melancholia

Endocrine therapy after menopause.—N. O. Rothermich, Beatrice Postle, and L. M. Foltz conclude that endocrine therapy of classical involucional melancholia is of doubtful value. They gave large doses of oestrogen and androgen to 24 patients showing depressive psychoses associated with, or after the menopause. In 14 patients presenting the classical picture of involucional melancholia the rate of improvement was little greater than that which generally occurs spontaneously. In 10 patients, however, with an involucional psychosis with atypical features, 70 per cent improved to such extent as to be able to return home and carry on a quite normal social existence.

Pre-frontal lobotomy

H. W. Woltman, B. F. Smith, F. P. Moersch, and J. G. Love report the successful performance of pre-frontal lobotomy to divide the subcortical association fibres in the frontal lobes and thereby remove the inhibitory function of the anterior poles of the cerebral hemispheres. This was one of 6 patients operated upon by the last-named (J. G. L.), a woman, aged 43, who had been in the Rochester State hospital with a diagnosis of 'agitated depression'. This form of treatment, successfully initiated by E. Moniz in 1936, has been carried out by J. W. Watts and W. Freeman, and by Grant and J. G. Lyerly. Lyerly's technique was followed, consisting of the elevation of a button of bone in each frontal region, 3 centimetres from the median line (superior sagittal suture) and 3 to 4 centimetres anterior to a line passing upward from each external auditory meatus and crossing the vertex. After reflexion of the dura mater a small incision is made in the cortex in a relatively non-vascular portion of a gyrus; the deep association fibres are then cut under direct vision by means of a Killian nasal septum elevator. It is specially insisted that the authors do not wish to advocate a surgical attack on the brain of every psychotic patient.

Caplan, G. (1941) *Brit. med. J.*, **1**, 479.

Lyerly, J. G. (1939) *Sth Surgeon*, **8**, 426.

Moniz, E. Quoted by Watts and Freeman.

Mott, F. W. (1919) *Brit. med. J.*, **2**, 655, 737.

Reiss, M. (1940) *J. ment. Sci.*, **86**, 767.

Rothermich, N. O., Postle, Beatrice, and Foltz, L. M. (1941) *Arch. Neurol.*

Psychiat., Chicago, **45**, 752.

Watts, J. W., and Freeman, W. (1937) *Sth med. J.*, **30**, 23.

Woltman, H. W., Smith, B. F., Moersch, F. P., and Love, J. G. (1941) *Proc.*

Mayo Clin., **16**, 200.

Young, G. C. (1941) *Lancet*, **1**, 12.

PSYCHOSES: PARANOIA AND PARANOID STATES

See also B.E.M.P., Vol. X, p. 292; and p. 79 of this volume.

Clinical Picture

C. W. Miller, Jun., reviews 400 cases of paranoid disorders to illustrate their general symptoms. The cases included paranoid schizophrenia, other forms of schizophrenia, senile and arteriosclerotic psychosis, involucional psychosis and some cases of syphilis, mental deficiency, epilepsy and psychoses due to alcohol and trauma. Nevertheless there were some common features in most of the cases, these being unsatisfactory marital and sexual adjustment; asocial tendencies, uncontrollable temper, projection tendencies, jealousy, introspection, and

rigid pride; indifference to religion, but a fanatical interest when it existed at all. Over 50 per cent of the patients had a normal childhood and in 30 per cent of them psychoses developed suddenly. The reaction of patients to their difficulties varied, and included violence, consultation of others for help, fright sometimes with suicidal attempts. Gross environmental factors, family attachments, and family constellations did not appear to be relevant. Prognosis appeared to be less favourable in the patients with fixed delusions. Recovery without insight was common, particularly in patients with only incidental paranoia. Prognosis was also better in cases of delusions removed from reality. It is emphasized that there is no paranoid disease as such and no single cause of paranoia, but that the symptoms can be precipitated or aggravated by difficult situations or physical factors.

Miller, C. W., Jun. (1941) *Arch. Neurol. Psychiat., Chicago*, **45**, 953.

PSYCHOSES: SCHIZOPHRENIA

See also B.E.M.P., Vol. X, p. 302; Cumulative Supplement, Key No. 1321; Surveys and Abstracts 1939, pp. 116 and 499; 1940, pp. 58 and 489; and p. 79 of this volume.

Definition and Nomenclature

New classification concept

R. L. Osborne criticizes the nomenclature of the condition called dementia praecox by Morel in 1856, and in 1910, by P. E. Bleuler, schizophrenia, terms which, when used indiscriminately and interchangeably, create additional confusion in a situation already extremely complicated. Further, Kraepelin's four types are also regarded as unsatisfactory, as half the cases are atypical for its divisions. A new classification is suggested: the term palaeophrenia (Greek *παλαιός* = ancient, *φρήν* = mind) should be confined to simple schizophrenia with symptoms or a history of archaic thought; in some cases there are transient delusions and fleeting hallucinations of a disagreeable nature. There may be mannerisms and bizarre behaviour as well as negativistic manifestations. Abstract thinking is diminished. Many cases now called simple schizophrenia show few or no symptoms of schizophrenia and should be classified under other headings ranging from psychopathic personality to primary behaviour disorders. The cases now known as paranoid schizophrenia should be divided into two main subdivisions: (1) those without evidence of archaic thought and due to a mechanism quite distinct from that of flagrant schizophrenia; these cases belong to a better organized form of paranoia, and this group should include those now called paranoia, some of those known as paranoid condition, and a few of paranoid schizophrenia; (2) those here called palaeophrenia, thus suggesting regression to a more primitive level.

Treatment

Leptazol shock therapy

Fractures of spine.—G. R. Krause and C. L. Langsam review the occurrence of fractures of the vertebrae after leptazol (cardiazol) treatment. A review of the recorded reports shows a high incidence of such fractures. Seventy-five patients were examined by X-rays before and after leptazol therapy; 32 of these (42.6 per cent) showed vertebral fractures. The most frequent sites of fracture were in the mid-thoracic region (68 out of 70 fractures). The 4th, 5th, 6th, and 7th vertebrae are particularly vulnerable. The thoracic region is rigid and subject to great muscular pull during convulsions, but no definite reasons for the fractures can be advanced. Patients with osteoporosis are very susceptible to fractures. The authors recommend X-ray examinations of the vertebral column before and after leptazol therapy and a safer method of treatment as an alternative to it. The use of curare is suggested as a possible prophylactic against fractures.

Bilateral fracture of femoral neck.—S. Androp reports a case of bilateral fracture of the femoral neck in a man, aged 43, caused by leptazol-induced convulsant shock therapy. Before the accident two convulsions were induced, one with 5 cubic centimetres of a 10 per cent solution of the drug, and the other with 6 cubic centimetres. Both were severe tonic and clonic generalized convulsions, lasting 45 seconds. During a third convulsion, at the end of a very severe tonic phase lasting about 20 seconds, a sharp snap was distinctly heard. Upon recovery from the attack the patient was unable to stand, and X-rays showed the fractures. The author suggests that the catatonic state of this patient with muscular rigidity might have had a bearing on the occurrence of the fractures.

Compressional fractures of the spine.—D. Blair reports that, of 6 patients treated by leptazol (cardiazol) convulsant therapy in whom vertebral fractures were found on X-ray examination, 4 had not any symptoms, and the other 2 complained of transitory backache only. Of 20 patients with severe epilepsy examined radiographically, 1 showed a vertebral fracture resembling those seen in convulsant therapy, and 3 others vertebral changes resembling those seen in convulsant therapy. The author considers that although the various vertebral mishaps reported in convulsant therapy cannot be ignored, their effects are not sufficiently serious to justify the abandonment of this method of treatment.

S. Androp, E. S. Margolin, J. H. Marshall, and Miriam Rittenhouse report 7 cases of vertebral compression fractures due to muscular action during convulsions induced by leptazol shock therapy, in 30 patients. There were 6 men and 1 woman, between the ages of 28 and 50. Each patient received between 7 and 20 injections of leptazol which caused convulsions of a moderate or severe nature. Three of the patients did not complain of any symptoms suggesting

a fracture; 3 others complained of tenderness and pain in the region involved, radiating along the spinal nerve roots, and lasting for from 3 days to 2 weeks. In one of the patients the discomfort lasted for more than a year, making it necessary to wear a corset. In another patient the patellar reflexes became unequal, the inequality lasting about 10 days. The onset was sudden, the convulsion lasting on an average 1 minute and passing through a succession of clonic-tonic-clonic stages.

Memory defects.—E. Ziskind reports 4 cases in which moderately severe defects of memory followed leptazol treatment, and 20 in which less marked changes occurred. As a rule the defect is minor in character and transient, and may even escape detection if not looked for. In the mildest form there is lacunar disturbance for isolated events of recent origin. In more severe cases remote memory is also affected. In still more pronounced forms Korsakow's syndrome may ensue. Other abnormalities in the more severe cases are impaired sensorium, silliness, neglect of personal appearance, mental retardation, emotional lability, perseveration, and feelings of familiarity. These associated symptoms, analogous to those observed in psychiatric pictures due to lesions of the brain, are significant, since they are readily recognized as being due to the treatment, and not as part of the disease. Recovery is the rule. Similarities in the loss of mental symptoms and the loss of memory under treatment suggest a common underlying mechanism. Both mental symptoms and memory tend to become effaced as therapy progresses. The effect on the symptoms, however, is greater in degree and earlier in occurrence than that on the memory. This is in conformity with the complete loss of symptoms after therapy, at which time memory is generally little affected. The degree of memory impairment is related to the number of leptazol convulsions. Two treatments a week for 6 to 8 weeks is fraught with little or no disability. Arteriosclerosis and toxicity call for caution, and possibly for fewer treatments. The use of sedative drugs, such as barbiturates, may predispose to memory defects. The author concludes that, since the memory impairment is reversible in almost all patients, this complication does not constitute a contra-indication to leptazol therapy.

In cardiovascular patients.—R. Good reports on 6 psychotic patients with cardiovascular disease treated by leptazol convulsant therapy, without untoward effects on the already damaged cardiovascular system. He concludes that, provided such patients have good compensation, and whether the severe cardiovascular disease exists alone or in the presence of advancing years and of diseases of other systems, leptazol convulsant therapy is not contra-indicated.

Results of treatment.—H. O. Colomb and G. L. Wadsworth analyse the results obtained with leptazol convulsant therapy in 97 cases of schizophrenia. There was a 50 per cent increase in the recovery rate over a standard control group of patients. The dosage employed at first was 3 cubic centimetres for females and 4 cubic centimetres for males of 10 per cent leptazol solution, but, because of some failures with fear reactions and later resistance, it was changed to 4 cubic centimetres and 5 cubic centimetres respectively. This dosage was maintained as long as a convulsion was produced, repeated immediately if necessary, and on the next occasion increased. It was possible to repeat doses of 10 cubic centimetres three times within 5 minutes without apparent ill effects. No serious complications occurred, except for the reactivation of quiescent pulmonary tuberculosis in 4 patients. It was found that, in favourable cases, the duration of the illness was shortened. Recovery occurred chiefly in patients who had been ill for less than a year, whereas patients whose illness was of longer duration did not seem to show any final material improvement. Patients in whom good results were obtained began to improve with the first five convulsions, and those who did not improve with the first five were not benefited by many convulsions. The authors suggest that patients who manifest the following characteristics should show the best results from the use of leptazol: (1) pre-psychotic personality within average limits; (2) individual previously adjusted from social and economic viewpoint; (3) acute onset; (4) duration of less than a year before admission; (5) prominent situational factors; (6) affective features, especially fear, depression, and tension states; (7) sensorium interference, particularly confusion and delirious states; (8) over-activity, mutism, and negativism; and (9) rapid regression.

Insulin therapy

Economical war-time method.—J. S. McGregor and R. A. Sandison describe a method of carrying out insulin shock treatment of schizophrenia which does not necessitate the use of large quantities of sugar. In order to economize, the quantity of sugar necessary to terminate coma, given by the nasal tube, was first reduced, but this failed, as any amount less than 7 ounces was uncertain in its action. Finally the plan adopted to interrupt coma was the intravenous injection of 20 cubic centimetres of 33 per cent glucose solution, followed on recovery by a pint of a soup made by mashing potatoes and mixing them into a soup of the consistency of a thin gruel with milk and water. To economize insulin, protamine-zinc-insulin was given intravenously instead of intramuscularly, and thus reduced the amount of protamine-zinc-insulin necessary to induce coma on an average by 46.6 per cent.

Compression fractures of the spine.—P. Polatin, M. M. Friedman, M. M. Harris, and W. A. Horwitz found that, among 173 patients treated with insulin-shock therapy, 62, or 36 per cent, showed epileptoid convulsions. The greatest number of the convulsions occurred in the fourth or fifth hour of hypoglycaemia. Of 34 patients who received only insulin-shock therapy and who were available for X-ray examination of the thoracic spine, 20.5 per cent showed compression fractures of the vertebrae. The incidence was higher in males than in females.

Of 12 patients treated with both insulin and leptazol who were available for X-ray examination of the spine, 3 showed compression fractures of the vertebrae. Maintaining the patient in the position of acute flexion while giving leptazol failed to prevent fractures. Two patients with negative X-ray evidence after convulsions during insulin-shock therapy subsequently showed no evidence of injury to the vertebral bodies.

Intravenous administration.—M. Jones compared the effect of insulin given intravenously with the usual intramuscular method of administration in the treatment of schizophrenia. He found that, to induce coma, the same amount of insulin was required by the intravenous as by the intramuscular route. By the intravenous route coma is produced sooner than by the intramuscular route; in 7 cases the average shortening of time was 45 minutes. One patient who was coma-resistant with intramuscular insulin remained so to intravenous insulin, even when a dose of 600 units was given.

Leptazol and insulin-shock therapy

Effect on cerebrospinal fluid proteins.—G. R. Kingsley and H. Freed found that both insulin and leptazol therapy caused appreciable changes in the protein of the cerebrospinal fluid in schizophrenic patients. The immediate effect of leptazol was a lowering of the albumin-globulin ratio. After 1 to 8 weeks of treatment and a rest of 3 or 4 days, the albumin and albumin-globulin ratio increased, whereas the globulin decreased. Insulin caused a rise in globulin and a depression of the albumin-globulin ratio. When the treatment was discontinued the albumin-globulin ratio increased and the globulin decreased.

Faradic shock therapy

N. J. Berkwitz treated 73 patients with various mental disorders, by faradic shock therapy, followed by the intravenous injection of pentothal sodium. The results obtained equalled those from other kinds of shock therapy. More striking results were obtained in conditions in which the personality was acutely and more or less totally involved, as in paranoid and catatonic schizophrenia, than in conditions in which it was partially involved, as in psychoneuroses, over a long period. Five patients with schizophrenia had relapses after treatment, but all responded quickly to further treatment. Faradic shock treatment does not produce as profound physiological changes as other forms of shock therapy, but is more controllable, safer, and relatively simpler and less expensive in use. From 10 to 20 daily treatments were given in most cases.

Electrical convulsant therapy

In a preliminary paper E. B. Strauss and A. Macphail report encouraging results in the treatment of out-patients by electrical convulsive therapy with a new portable apparatus. In all, 18 patients mainly attending the Department of Psychological Medicine at St. Bartholomew's Hospital, and most of them unsuitable for admission to a mental hospital, were treated, including cases of hebephrenia, paranoid schizophrenia, the schizophrenic type of depression, schizophrenia simplex, manic-depressive psychosis-mixed phase, manic-depressive psychosis with nihilistic delusions and corresponding somatic hallucinations, stuporous melancholia, involutional melancholia, manic-depressive psychosis, hypochondriacal type complicated by morphinism, schizoid psychopathy with acute anxiety symptoms, schizophrenia with alcoholism, and multiple tics. The voltages used varied from 80 to 100, the time of passage of the current through the patient from one-tenth to one-half second.

Triazol convulsant therapy

Fatal cerebral fat-embolism.—G. S. Nightingale and A. Meyer report the case of a married multipara, aged 33, with schizophrenia, who was given 5 intravenous injections of leptazol (cardiazol) from October 17 to November 3, 1939, and then 18 injections, all but the first and the last intravenous, from November 8, 1939, to January 12, 1940, of triazol (hexazole, azoman). After a typical epileptic fit followed by coma, lasting 12½ hours, death occurred, with cyanosis, dyspnoea, and moist râles at the bases of the lungs. This was the only fatality among 59 cases thus treated at the Brentwood Mental Hospital since July 1938. At the necropsy, the account of which is accompanied by 9 illustrations, the kidneys were congested and showed cloudy swelling, the liver was moderately fatty, and the lungs showed patches of haemorrhage and terminal oedema. The meninges showed intense venous stasis, and the right frontal lobe, an area of haemorrhagic softening the size of a walnut. Histological examination and staining with scarlet-red established the wide-spread presence of fat emboli in the cerebrum and cerebellum. There was thrombosis of the arteries of the circle of Willis, but not any arteriosclerotic or syphilitic changes in the arterial walls. In a full discussion of such an exceptional sequence of events after this form of treatment, it is pointed out that there was not any evidence of bone fracture, which is the common cause of fat embolism, although vertebral fractures may be overlooked, and such an accident does not appear to have been suspected at the time of the necropsy. There are other causes, such as damage to subcutaneous fatty tissue, and the patient showed bruising of the skin before death. Although cutaneous petechiae, a recognized diagnostic sign of fat embolism, was absent, the presence of cerebral fat-embolism was convincing. Further, it is suggested that if looked for in fatal cases of convulsive treatment, it may not be so exceptional.

Ammonium chloride convulsant therapy

E. C. Dax reports on the use of ammonium chloride injected intravenously as a convulsant in 24 patients; nearly all females. It was hoped that the treatment, introduced by Bertolani and employed in 27 cases of acute schizophrenia by Mazza, would be free from some of the

ill effects of other convulsant drugs such as leptazol (cardiazol) and azoman (hexazole, triazole), and give comparable results, but it does not appear that it has been completely successful in these respects. No sedatives are given during the 12 hours before injection of 10 cubic centimetres = $7\frac{1}{2}$ grains of a 5 per cent solution. Four stages in the fit are described: (1) preliminary; in about 5 seconds after the injection the patient is apprehensive and complains of a bitter taste in the mouth before losing consciousness; (2) 10 to 20 seconds after the injection hyperpnoea, dilatation of the pupils, and deviation of the head and eyes appear; (3) convulsions suddenly take the place of hyperpnoea and deviation of the head, and are never so severe as those induced by leptazol and by azoman; this stage lasts 10 to 20 seconds; (4) recovery; after 5 or 10 minutes the patients are able to sit up and many to get up soon after. The systolic blood pressure is not more than half that observed with azoman or leptazol; the diastolic pressure rarely rises by more than 10–15 millimetres of mercury and is sometimes unchanged. The pulse rate may reach 180 during the fit, but usually settles within 3 minutes after the convulsions have ceased. Although patients much prefer ammonium chloride to leptazol and to azoman as a convulsant, they do not like it. Although the dangers of fractures are negligible, the general results are not so satisfactory as those of leptazol and of azoman; it may be regarded as useful in patients who have not responded to other convulsants. Of the 25 patients 10 were schizophrenics; 1 had cardiac failure after the treatment.

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PSYCHOSES: ALCOHOLIC PSYCHOSES

See also B.E.M.P., Vol. X, p. 332; and Surveys and Abstracts 1939, p. 505; 1940, p. 497.

Korsakow's Syndrome

Wernicke's polio-encephalitis

Associated with vitamin B deficiency.—A. C. P. Campbell and W. R. Russell analyse 21 fatal cases, confirmed by necropsy, of the condition described by Wernicke in 1881 as acute superior haemorrhagic polio-encephalitis. Twelve of these cases had been utilized by Campbell and Biggart (1939) from a pathological point of view and led to the following conclusions. The lesions consist of foci of vascular stasis and parenchymatous degeneration, occurring symmetrically in the corpora mamillaria, and also, though not always, in other parts of the hypothalamus, the fornix, the juxta-ventricular zone of the thalamus, the grey matter round the aqueduct of the midbrain, the posterior colliculi, and the floor of the fourth ventricle. Campbell and Russell consider that the condition is not rare, and occurs in a number of other primary diseases nearly always involving chronic gastro-intestinal disorder. The traditional cause, alcoholism, with its greatly reduced intake of food comes into this category; among the 21 cases it accounted certainly for 5 and possibly for 8; this suggests vitamin deficiency, probably some part or parts of the B complex. The therapeutic results from nicotinic acid suggest that its deficiency may play some part, but deficiency of vitamin B₁ complex appears to be more important than that of B₂. The duration of the disease in the 21 cases varied from 1 day to 10 weeks, averaging 17 days. Although it is usually fatal, evidence of recovery is brought forward, including a case after treatment with vitamin B. The clinical features fall into two categories: (1) disturbance of consciousness and of the higher cerebral functions: Korsakow's psychosis is an important feature here, and is said to be always accompanied by Wernicke's disease; and (2) local neurological signs and symptoms, the most important of which are oculomotor disturbances.

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PUERPERIUM

See also B.E.M.P., Vol. X, p. 365; Cumulative Supplement, Key Nos. 1326-1329; Surveys and Abstracts 1939, pp. 31 and 507; 1940, p. 497; and p. 22 of this volume.

Physiology of the Puerperium*Involution*

Effect of stilboestrol on post-partum uterus.—H. F. Connally, Jun., D. I. Dann, J. M. Reese, and L. H. Douglass report on the administration to 200 puerperal women of diethylstilboestrol in order to show the effect of oestrogens on the post-partum uterus. None of the women showed any toxic effects, even though the drug was given in larger doses than usual. Uteri sensitized by the drug appeared to respond more readily than controls to oxytocics. In 70.5 per cent of the cases lactation was apparently suppressed. In the dosage employed complete inhibition was not noted, although the onset of lactation was delayed longer than in the control group. Engorged or painful breasts were not noted. The flow of lochia was not materially changed. Stilboestrol apparently had no immediate effect on early involution of the puerperal uterus, though pelvic examinations on about the twenty-first day post-partum showed a more rapid involution than in the control group.

Management of the Normal Puerperium*Ergometrine treatment*

J. B. Lounsbury gave ergometrine to 100 primiparas and multiparas, during the first 3 days of the post-partum period. A further 100 patients served as controls. The dosage was 0.2 milligram hypodermically, after delivery of the placenta, and 0.4 milligram orally 6 hours post-partum. For the next 3 days 0.2 milligram was given by mouth 3 times a day. The drug increased the rate of involution of the uterus, produced a more regular rate of involution with fewer periods of greater or lesser subinvolution, diminished the amount and the sanguineous character of the lochia, and reduced the puerperal morbidity due to uterine infection.

Puerperal Sepsis*Treatment*

Sulphonamide compounds.—W. Filler successfully treated a case of puerperal sepsis due to *Staphylococcus aureus* with sulphamethylthiazole. The dosage employed was 2 grammes by mouth followed by 1 gramme every 4 hours; 5 grains of sodium bicarbonate were given with each dose of the drug. A total dosage of 88.6 grammes was given and after this the organism disappeared from the blood. The patient made a good recovery and was discharged from hospital well.

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PYLORIC OBSTRUCTION

See also B.E.M.P., Vol. X, p. 426; Surveys and Abstracts 1939, p. 509; 1940, p. 501; and pp. 4, 13, and 50 of this volume.

Hypertrophic Stenosis of the Pylorus*Treatment*

Eumydrin.—R. H. Dobbs treated 40 patients with congenital hypertrophic pyloric stenosis with eumydrin (atropine methylnitrate); of these 13 were discharged within 10 days; these infants were all 4 weeks old, or more, before vomiting began; 10 showed some response within 10 days and were discharged within 3 weeks after admission; 4 were discharged after 30 days; and 12 had not responded within 12 days, and were treated surgically. The findings suggest that those patients with pyloric stenosis in whom vomiting has not occurred until after the fourth week of life can be safely treated as out-patients, and a rapid response may then be expected.

Helen M. M. Mackay treated 40 consecutive cases of hypertrophic pyloric stenosis with eumydrin (atropine methylnitrate). Of these, 31 patients were cured by the drug and 4 more by operation. Five patients died, and 4 of these deaths were due wholly or in part to enteritis contracted in hospital and 1 was probably due to excessive fluid administration. Of 5 patients who did not respond to the drug, all received a high fluid intake which probably prevented the drug from effecting relaxation of the pyloric spasm. Excessive fluid intake was also accompanied by a less rapid response to eumydrin, a slower gain in weight, and often by poor appetite. No obvious benefit ensued from routine gastric lavage. In 35 cases there was disappearance of, or reduction in, the pyloric obstruction as a result of eumydrin treatment, and in the cases definitely cured by eumydrin therapy, vomiting was markedly diminished in an average of 2.9 days and the babies gained in weight, on an average 6.8 ounces in the first week, and 6.9 ounces weekly for the first 5 weeks. The most serious toxic effect was abdominal distension, which could be obviated by early reduction in dosage. The dosage rose 0.05-1 cubic centimetre of a 1 in 10,000 aqueous solution of eumydrin, to 2-3 cubic centimetres given orally before each of 6, or occasionally 7, feeds in 24 hours. This amounted to 1.2 to 4.2 milligrams of eumydrin daily. In 1 case the drug was given by lingual application of an 0.6 per cent alcoholic solution; a dosage of approximately 0.2 milligram every 24 hours,

given twice daily, was followed by immediate reduction in vomiting. The author suggests that temporary relief of the pyloric spasm may possibly break a vicious circle, and makes a plea for the more wide-spread adoption of eumydrin therapy in this condition.

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RADIOLOGY IN DIAGNOSIS AND TREATMENT

See also B.E.M.P., Vol. X, p. 456; Cumulative Supplement, Key Nos. 1340-1343; Surveys and Abstracts 1939, pp. 18, 23, and 511; 1940, pp. 94, 98, and 502, and p. 71 of this volume.

Methods of Radiography

Contrast media

Sodium thorium tartrate.—F. R. Greenbaum and A. F. Peters report on a new organic thorium compound, sodium thorium tartrate, as a diagnostic agent, particularly for the gastro-intestinal tract. It was prepared as follows: 48 grammes of thorium nitrate were dissolved in 100 cubic centimetres of water; 67.2 grammes of tartaric acid were also dissolved in 100 cubic centimetres of water. The tartaric acid solution was added to the thorium nitrate solution; 300 cubic centimetres of denatured alcohol were then added, the thorium tartrate being precipitated from the solution as a gelatinous mass. This was filtered off, washed with denatured alcohol, and dried, giving about 50 grammes of insoluble thorium tartrate. To the thorium tartrate suspended in 100 cubic centimetres of distilled water was added 10.8 grammes of chemically pure sodium hydroxide, dissolved in 10 cubic centimetres of water. The solution was filtered and precipitated with alcohol-acetone mixture. The precipitate was dried and gave 53 grammes of sodium thorium tartrate. Experiments on rabbits showed a complete absence of toxicity, when the drug was given by the stomach over a period of more than 60 days; it seemed to be rapidly eliminated. After a dose of 10 or 20 cubic centimetres of the drug by mouth, the stomach of rabbits was clearly outlined, the image being clearer than when barium sulphate was employed.

Uroselectan B in excretion pyelography

Thrombosis of injected veins.—F. H. Kemp discusses the relation between the intravenous injection for excretion pyelography, of uroselectan B and similar preparations, and thrombosis of the injected veins. In a clinical investigation of the effects of a British preparation of uroselectan B it was found that the immediate effects were trivial, but if the patients were re-examined 10 to 14 days later, a significant number was found to have thrombosis of the injected veins. Although this has long been known, it may be more frequent than is generally realized. In patients injected, painful arms only occurred in out-patients, and presumably the other patients were benefited by rest, for venous thrombosis was not confined to those who had pain. It is probable that the risk of venous thrombosis may be diminished by slow injection with minimum damage to the vein wall. When pain is felt along the course of the veins at the time of injection, it is conceivable that the veins are hypersensitive to the preparation.

X-ray examination of air-raid casualties

Foreign bodies.—M. E. Samuel states that in the investigation of air-raid casualties most information concerning the position and number of foreign bodies is obtained by the use of X-ray films rather than by screening methods. The expense of the method is justified by the minute disturbance necessary to obtain this information with a portable unit. The skull and chest should always be X-rayed immediately, if there is any suspicion of injury to either of these regions, as by no other means can information regarding lesions in these regions be accurately obtained.

Systematic Radio-Diagnosis

Skeletal system

Suprasternal bones.—H. Morris reports a case in a man, aged 32, with subacute arthritis of the left ankle and vague pains elsewhere and in the middle of the sternum, in whom two suprasternal bones were demonstrated radiologically. In a review of the subject the author adds that these suprasternal or episternal bones were found in 3 per cent of cadavers examined radiologically, but are seldom detected during life (Cobb). They are regarded as persistent remnants of the epicoracoids of the primitive shoulder girdle, vary in size from that of a grain of barley to that of a hazel-nut, and show the same structure as that of the sternum with which they are fused in about 60 per cent of the cases (Cobb). They appear to be an isolated abnormality and not associated with cleft sternum or cervical rib.

Nervous system

Myelography with iodized oil.—A. W. Marcovich, A. E. Walker, and C. M. Jessico state that the intrathecal injection of iodized oil is followed in more than 50 per cent of cases by a mild fever of short duration, and less often by headache and aggravation of previous symptoms. The cellular and protein contents of the cerebrospinal fluid are generally increased for a few days. Permanent clinical ill effects from the injection of 2 to 4 cubic centimetres of iodized oil are very rare. Although the oil gradually becomes fixed in the sheaths of the spinal nerves and the caudal sac, it generally produces only mild arachnoiditis with fine adhesions between the arachnoid and the dura mater. Opening of the dura after injection of iodized oil may cause the oil to become encysted by proliferation of the arachnoid. The presence of small globules of oil in the intracranial cavity does not appear to produce any symptoms.

Renal tract

Kidney.—S. Nowell reports on 3 cases which, on excretion urography, showed an increasing density of one kidney shadow. In 2 of these cases the pelvis and calyces of the same kidney were not demonstrated, and in each a stone was present in the corresponding ureter. It was considered that the cause of the increased density was retention of the contrast medium in the kidney tubules, owing to the pressure of the urine held up in the renal pelvis during the acute phase of a ureteric obstruction.

Radiotherapy**X-ray therapy**

Effect on Jensen's rat sarcoma.—S. Russ and G. M. Scott found that, when a dose of X-rays, approximately 1,200 roentgens, was given to the surrounding tissue of a rapidly growing Jensen's rat sarcoma, the rate of growth of the tumour was considerably slowed down, and nearly 37 per cent (actually 30 out of 82 tumours) disappeared. The amount of damage to the skin caused by this dose was negligible, nothing more than a slight temporary depilation in some cases. The number of untreated control tumours which spontaneously disappeared was 13 out of 190 (just under 7 per cent).

Harmful effects of deep X-ray therapy on a malignant bronchial tumour.—V. C. Jacobsen reports a case of extra-pulmonary carcinoma of a bronchus in a patient treated by deep X-ray therapy for 9 years, during which he had received a total of about 18,300 roentgens. At necropsy the tumour was found almost entirely destroyed, a small remnant being apparently held in check by this treatment. A productive pleurisy, however, had ensued and was followed by much atelectasis, chronic interstitial fibrosing pneumonitis, and chronic bronchitis with haemoptysis from intra-bronchial granulations. A marked degree of obliterative change occurred throughout the arterial tree of the affected lung. The author states that, while radiotherapy of pulmonary carcinoma is of value, the pleural and pulmonary damage which may result from such measures should be appreciated, and guarded against as much as possible.

Radionecrotic ulcers: zinc treatment.—B. S. Freeman, studying bacteriologically 35 cases of radionecrotic ulcers with and without persistent tumour growth, found a predominance of anaerobic organisms. Infection in such ulcers may obscure the persistence of tumour tissue, not only grossly, but histologically. The author employed zinc peroxide to control foetor, infection, and pain in such cases. The method of application was as follows: the wound was cleaned with peroxide and saline sprays, free necrotic tissue was gently removed, and the wound again sprayed. Zinc peroxide, which had been previously sterilized by baking at 140° C. for 4 hours in a dry oven, was mixed with sterile water, added until a cream was formed. The mixture was applied by means of a syringe to the lesion. Fine-mesh gauze was soaked in the suspension and applied throughout the lesion and into all the sinuses and interstices of the wound. The whole was covered with sterile pads soaked in distilled water, and the wound was packed, to prevent evaporation, with several layers of petroleum jelly or zinc oxide gauze. Dressings were changed once a day. In the treatment of oral lesions and of necrotic bone lesions, the zinc peroxide was applied as a thick paste, every 3 hours, and 1 in 3 suspension was employed as a mouth wash. A mouth wash of zinc peroxide was employed during pre-operative dental prophylaxis, to prevent or diminish the frequency or degree of irradiation bone necrosis in lesions of the mucous membrane.

Toxic effects on blood.—D. I. Macht found that specimens of blood obtained from patients after X-ray treatment had been given showed a marked toxicity from 24 to 48 hours after irradiation. This toxicity was shown in blood from patients with both malignant and non-malignant pathological conditions, so that it could not be ascribed to resolution of tumours and absorption of their products of decomposition.

Effect on serum cholesterol level.—Barbara E. Holmes, working in the laboratories of the Imperial Cancer Research Fund on the blood serum of patients irradiated with X-rays for malignant disease at Mount Vernon Hospital, confirmed the conclusions of Burgheim (1927), (1) that the most usual reaction of the blood cholesterol after the first and often after the second irradiation was a rise in the serum cholesterol, ascribed to the release of cholesterol from the irradiated tumour, and (2) that in patients with irradiation sickness there may be a tendency for the serum cholesterol level to fall. Any direct relation between the amount of cholesterol in the serum and the symptoms observed, or any definite time-relation between the two cannot be substantiated, this probably explaining why some workers have not confirmed Burgheim's results. Holmes concludes that some factor concerned with the production of the symptoms may tend also to cause a metabolic change leading to a loss of cholesterol from the blood.

Effect on small intestine.—W. S. Wallace found that in a group of patients with carcinoma of the cervix, examination of the small intestine before and after a protracted series of high-voltage X-irradiations of the pelvis showed that, though the duodenum and jejunum were not greatly altered, the ileum showed marked changes which included segmentation of the barium stream, flattening of the mucosal pattern, and diminished motility and narrowing of the lumen.

Radio-sensitivity of tumours.—S. Warren, in a discussion on the radio-sensitivity of tumours, classifies these into three groups as follows: (1) radio-sensitive growths which regress strikingly or disappear clinically with a total X-ray dosage of 2,500 roentgens or less of protracted radiation; (2) radio-responsive growths which require from 2,500 to 5,000 roentgens for

similar regression; (3) radio-resistant growths which require more than 5,000 roentgens for response. In the first group, which includes lymphomas, chronic leukaemia, and Ewing's tumour of bone, normal tissue in the field of radiation will show appreciable damage; in the second group, which includes tumours such as basal-celled carcinoma of the skin, cancer of the cervix, and adenocarcinoma of the thyroid, normal tissue will show definite reactions, but will generally recover without permanent severe injury; in the third group, which includes carcinoma of the stomach, cancer of the breast, malignant melanoma, and osteogenic sarcoma, damage to normal tissue may equal or even exceed the damage done to the growth.

Radium therapy

Birth-marks.—J. E. Breed recommends surface radium therapy for birth-marks; its careless use, however, might result in undesirable sequelae such as ulcerations, scars, atrophy, telangiectasia, and recurring radium dermatitis. The advantages of radium therapy are that it is painless and that treatment may be begun in earliest infancy; in selected cases the results are excellent. Cosmetic success depends on the avoidance of inflammatory reactions.

Clinical applications

In various diseases.—C. J. Smyth, R. H. Freyberg, and W. S. Peck treated 100 patients with local high-voltage X-ray therapy. In a large group with rheumatoid arthritis, 44 per cent did not show any subjective or objective benefit; in 30 per cent only subjective benefit occurred, and only in 26 per cent was there any objective improvement which could be attributed to X-ray therapy. There were significant subjective and objective results in 74 per cent of 15 patients with rhizomelic spondylitis. In some instances the symptoms completely disappeared, and in 2 with early spondylitis clinical evidence of the disease had almost entirely passed off.

Skin.—A. C. Cipollaro advocates more uniformity between dermatologists and radiologists in irradiation methods for skin diseases, although no rigid standard can be adopted. Unfiltered rays generated with 50 kilovolts are considered to be adequate for routine therapy of diseases which will respond to 100 kilovolt rays. High-voltage filtered rays may be harmful as well as unnecessary. Grenz rays have low penetration and are useful only for treating recurring eczema or psoriasis in hairy regions and for lesions of the eyelids and scrotum, and for some special diseases. General antiseptic hygienic treatment is suggested for acne vulgaris and dermatophytosis with unfiltered rays of 75 roentgens at a low voltage. For neurodermatitis and psoriasis radiation should be applied with extreme caution in weekly doses of unfiltered rays of 75 roentgens at a low voltage, and for generalized psoriasis only rays of 40 roentgens are required. There is danger of recurrence and sequels, and different parts of the body should be irradiated at each sitting. Not more than 6 treatments should be applied to the nails in 1 year. Mycosis fungoides can be checked but not cured by careful irradiation, and when found in the gastro-intestinal tract, lungs, bones, and lymphatic glands, high-voltage filtered rays may be used. Low voltage unfiltered irradiation may alleviate verrucae, but there is a danger of chronic radiothermic ulcers due to the over treatment of plantar warts. Corns and callosities are objects for mechanical adjustment, not irradiation. Keratoses usually respond to irradiation and so do keloids once they appear. Irradiation is inadvisable in cases of hypertrichosis; electrical treatment is adequate. In the discussion, J. R. Driver and I. S. Trostler insisted on the danger of excessive irradiation, and the former urged special discretion in its use in children.

Experimental irradiation of skin.—B. Jolles found that, on irradiating the skin of the rat under constant physical conditions, but with fields of various sizes, the extent of the field influenced quite profoundly the degree of reaction of the skin. The larger the area irradiated, the more severe was the damage done, even though the dose of X-rays given per unit area was kept constant. Further experiments show that the reaction becomes minimal when the normal tissues can exert their maximal protective influences; this has been arranged experimentally by surrounding the X-rayed area by as much normal tissue as possible.

Carcinoma of cervix uteri.—An account of their methods of irradiation in cancer of the cervix uteri is given by S. T. Cantril, F. Buschke, and H. M. Parker. Preliminary examination should determine anatomical limits of growth, effects of other diseases, and should include cystoscopy and intravenous urography. Lasting relief is not obtained by irradiation in the late stages. The idea of a standardized treatment is condemned. X-rays are given with an apparatus operating at 800 kilovolts, 10 milliamperes, 4 millimetres lead filtration, 100 centimetre distance, giving a skin intensity of 23.5 roentgens per minute on a field of 10 × 14 centimetres. Intra-uterine irradiation is given when the patient is free from fever. The length of the uterine canal is measured and the cervical dilatation should be minimal. The maximum intra-uterine charge employed is 40 milligrams (1 millimetre platinum filtration) using two 20 milligram sources for a canal of 5 or 6 centimetres, with additional sources in the ratio of 20 : 10 : 10 milligrams for longer canals (from fundus to external os). Vaginal application is made not more than 24 hours later with an applicator of the Manchester Holt Radium Institute type. The usual dose is 4,000 milligram hours in 4 or 5 days. The total dose aimed at is 8,000 milligram hours. Radium should be used where possible before X-rays when they are both used. Rectal reactions cannot be avoided, but the dosage should be reduced until diarrhoea subsides. When they appear near the end of treatment, the final dose must be given cautiously. X-ray therapy alone is effective only in radio-sensitive growths infiltrating down into the vagina. Two anterior suprapubic and two posterior lumbosacral fields are used

without tilting the pelvis. Six fields are sometimes used to lessen the surface dose on any one field if the total dose is beyond 12,000 roentgens. The ischio-sciatic field is less important in super-voltage therapy. This and all other fields require vaginal examination. Treatment is given daily through a single field. Pain during treatment necessitates rotation of the fields and an increased dosage. The inguinal folds can be blocked out. Certain complications may be avoided by an increased radium dose and a reduced X-ray dose over a long period. The unorthodox method of adding gamma irradiation to a measured X-ray dose helps to determine the quantity of total irradiation used. The size and approximate limits of the pelvic dose for different diameters are determined by a wooden model of a pelvis and isodose curves compiled from it. Uncontrolled parametrial disease resulting from combined ray and gamma irradiation may be controlled by either additional radium or X-ray treatment, the former in patients with a small pelvis, and the latter in patients with a large pelvis. The policy of completing X-ray treatment (except in stage IV) when conditions are ripe for radium, is mistaken. Increased dosage will not cure stage IV growths. The skin dose would have to be increased by 50 per cent to raise the pelvic dose from 3,200 roentgens to 5,000 roentgens.

Bronchiogenic carcinoma.—E. T. Leddy and H. J. Moersch employed X-ray therapy in 250 cases of proved bronchiogenic carcinoma, the prognosis of which was poor because a correct diagnosis was only made at the advanced stage of the disease. In spite of this the treatment gave marked palliation, and in 25 cases the patients lived for from 1 to 12 years. The authors conclude that any patient who is not in too precarious a physical condition should have at least one course of X-ray therapy, otherwise the expectancy of life is at most 1 year. Adenocarcinoma appeared to be more amenable to treatment than epithelioma.

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Wallace, W. S. (1941) *J. Amer. med. Ass.*, **116**, 583.

Warren, S. (1941) *Amer. J. Roentgenol.*, **45**, 641.

RAT-BITE FEVER

See also B.E.M.P., Vol. X, p. 477.

Clinical Picture

Fatal termination

J. Greengard and E. R. Hess report a case of rat-bite fever in an infant aged 11 days. This appears to be the youngest patient recorded with this disease. The first onset of fever was exactly 15 days after the bite. Four days before this the local lesion appeared at the site of the tooth perforations on the hand, with deep-seated induration, associated oedema of the thumb and index finger, and lymphadenitis involving the epitrochlear and axillary glands. With the onset of fever there was a generalized macular erythema which lasted several days. After an afebrile interval, a second bout of fever and erythema occurred, and an intercurrent respiratory infection led to a fatal termination.

Greengard, J., and Hess, E. R. (1941) *J. Amer. med. Ass.*, **116**, 2393.

RAYNAUD'S PHENOMENON

See also B.E.M.P., Vol. X, p. 486; Cumulative Supplement, Key No. 1345; and Surveys and Abstracts 1939, p. 518.

Clinical Picture

Special characteristics of the different conditions in which Raynaud's phenomenon occurs

In sclerodactyly (acrosclerosis).—P. A. O'Leary and M. Waisman analyse 64 cases of this combination of Raynaud's phenomenon with secondary scleroderma of the distal parts of

the extremities and of the face and neck, seen at the Mayo Clinic. Like Raynaud's phenomenon, acrosclerosis chiefly attacks females, beginning during adolescence or in adult life. The early symptoms are due to intermittent arteriolar spasm in the upper limbs and sclerodactyly; facial sclerosis may coincide with the appearance of sclerodactyly or it may be delayed for some years. The skin of the face is drawn, stretched, but not so hard as it is taut; the lips are thinned, shortened, and radially furrowed. The neck is sometimes involved and the sclerotic changes may invade the skin over the upper part of the chest, and the affected areas are occasionally much pigmented. The fingers become stiff and semiflexed with dystrophic changes going on to ischaemic ulceration and gangrene. Histologically the changes are those of scleroderma. Ten per cent of cases of Raynaud's phenomenon show involvement of the fingers with scleroderma. The progressive lesions of diffuse scleroderma are usually more advanced within 2 years and the prognosis more unfavourable than in acrosclerosis. In the latter condition the treatment suggested is by foreign protein intravenously, physical measures, and sometimes a prolonged course of pituitrin or mecholyl (acetyl- β -methylcholine chloride). But sympathectomy is not so successful as in Raynaud's phenomenon, presumably because of the obliterative changes in the blood vessels. The conclusion is reached that, although the mechanism is obscure, acrosclerosis is a form of Raynaud's phenomenon in which a number of trophic disturbances have become localized on the hands and face simultaneously with, or consecutively to, the vasomotor changes.

Scleroderma and pulmonary fibrosis in Raynaud's phenomenon.—H. Linenthal and R. Talkov report 3 cases of Raynaud's disease during the course of which scleroderma developed, with subsequent fibrosis of the lungs of unknown aetiology. It is suggested that the pulmonary fibrosis was secondary to changes in the small vessels of the lungs as part of Raynaud's phenomenon, and that this disease is therefore not limited to the arteries or the extremities and the digits, but may involve the arteries of the lungs and possibly of other organs.

Linenthal, H., and Talkov, R. (1941) *New Engl. J. Med.*, **224**, 682.

O'Leary, P. A., and Waisman, M. (1940) *Proc. Mayo Clin.*, **15**, 702.

RECTUM DISEASES

See also B.E.M.P., Vol. X, p. 502; Cumulative Supplement, Key Nos. 1346–1356; Surveys and Abstracts 1939, p. 519; 1940, p. 506; and p. 14 of this volume.

Internal Haemorrhoids

Treatment

Injection.—J. K. Anderson states that the contra-indications to the injection treatment of internal haemorrhoids are fissure, fistula, and a thin perineal floor, injection near which may result in a fistula, especially in multiparas. The disadvantages of injection treatment are that there are 10 per cent or more recurrences within a period of 5 years afterwards, that the lesion is not removed, that much time is required on the part of both physician and patient, and that complications are not infrequent.

Benign Tumours

Polyposis intestinalis

Differential diagnosis.—J. Felsen, in a discussion of the differential diagnosis of intestinal polyposis, states that adenomatosis of the colon is a neoplastic, miliary and discrete adenomatous condition studding the mucosa from the rectum to the ileocaecal valve. There is an undoubted hereditary tendency of the Mendelian type; the aetiology is unknown. True multicentric malignancy is a frequent aftermath. There is no mucosal ulceration or mural fibrosis. If stenosis is present, it is local and due to the size of the tumour, malignant change, or associated desmoplasia. There is no loss of haustration. The best treatment is complete colectomy. Polyposis cystica intestini is an inflammatory lesion and consists essentially of small islands of intact mucosa separated by linear and geographic areas of ulceration. It is a pseudo-polyposis and should be termed chronic ulcerative colitis. It is an acquired condition and represents the late phase of initial acute bacillary dysentery. Mucosal ulceration, mural fibrosis and stenosis often occur in a segmental manner and may involve the small as well as the large intestine. Loss of haustration is a characteristic X-ray sign and malignancy never ensues. The best treatment is the prevention of bacillary dysentery.

As precursor of carcinoma.—R. J. Jackman records the case of a man who, when 58 years old, was found to have two small polypi, each 5 millimetres in diameter, in the recto-sigmoid region; he declined fulguration, and 6 years later was seen with an inoperable carcinoma, grade 2 according to Broders's classification, with symptoms for three months. The adenocarcinoma obscured the site of the polypi. Whether or not all polypi of the colon which, like adenocarcinoma, are commonest in the rectum and sigmoid, will become malignant and whether sessile or pedunculated polypi are more likely to become malignant, are debatable questions. At present there is not any method based on morphology which can determine whether or not malignant changes will occur in a polyp. The ease of destruction of polypi in the rectum and sigmoid by fulguration makes this form of treatment most important. Polypi resulting from chronic ulcerative colitis and further carcinomatous change are regarded as frequent.

Carcinoma

Treatment

X-ray treatment without colostomy.—Ff. Roberts describes 4 cases of non-obstructive

inoperable cancer, and mentions that during the last 5 years he has treated 35 cases by X-rays without colostomy. He concludes that, except in advanced cases, in inoperable non-obstructive carcinoma of the rectum, X-ray treatment provides a method of restoring rectal function to a degree compatible with an active life for a considerable period, without resort to colostomy. It causes the minimum of discomfort, and avoids any operative procedure.

Anderson, J. K. (1941) *Clin. Med.*, **48**, 42.

Felsen, J. (1941) *Amer. J. Roentgenol.*, **45**, 551.

Jackman, R. J. (1941) *Proc. Mayo Clin.*, **16**, 11.

Roberts, Ff. (1941) *Brit. med. J.*, **1**, 357.

REFLEXES IN DIAGNOSIS

See also B.E.M.P., Vol. X, p. 558; and Surveys and Abstracts 1939, p. 520; 1940, p. 507.

Clinical Aspect

Babinski and crossed plantar responses

Interpretation of Babinski's sign.—K. Goldstein states that Babinski's sign is the expression of a change in the normal ratio of response to stimulation of flexor and extensor muscle. Contrary to the normal situation, under certain conditions the extensors become more easily excitable than the flexors, and therefore stimulation of the sole of the foot causes dorsal flexion of the big toe. The phenomenon occurs also in cases without pyramidal tract lesions, when for any reason the dorsal flexors are more easily excitable than the plantar flexors—as in some cases of poliomyelitis, muscular atrophy, and peripheral neuritis. The change in the normal ratio of responsiveness to stimulation of flexor and extensor muscles, if associated with a lesion of the pyramidal system, is an expression of reduced function of the motor system.

Goldstein, K. (1941) *J. nerv. ment. Dis.*, **93**, 281.

RETINA DISEASES

See also B.E.M.P., Vol. X, p. 611; Cumulative Supplement, Key Nos. 1364–1379; and Surveys and Abstracts 1939, pp. 130 and 522; 1940, p. 510.

Vascular Diseases

Venous thrombosis

Treated by heparin.—R. L. Rea treated 5 cases of thrombosis in the central vein of the retina with heparin; 3 of the patients had complete trunk thromboses and 2 had branch thromboses. In 1 case of trunk thromboses the treatment was unsuccessful, the eye becoming glaucomatous and blind; in the other 2 some improvement was evident. In the 2 patients with branch thromboses complete cure resulted, central vision being 6/6 in each. The dosage was 250 milligrams per day (equivalent to 5 cubic centimetres of a 5 per cent solution) given in 2 injections. One patient received a total of 30 cubic centimetres.

Varices

In diabetic retinitis.—C. S. O'Brien and J. H. Allen state that varices of the retina are uncommon, but are seen occasionally in patients with diabetes mellitus and diabetic retinitis, and more rarely in those with arteriosclerotic retinitis. In addition to the typical findings of diabetic retinitis with its commonly associated arteriosclerotic changes, the veins show irregular localized varicosities. Histologically the veins are sclerosed, their walls showing variations in thickness, hyaline degeneration, endothelial proliferation, and thromboses.

Retinitis Pigmentosa

Clinical picture

E. C. Dax records in full detail 11 cases of retinitis pigmentosa the pathological basis of which is now regarded as an heredo-degeneration of the nervous elements of the retina. The author reviews the subject, especially with reference to evidence of associated degenerative lesions, such as the Laurence-Moon-Biedl syndrome, deafness and deaf-mutism, skeletal abnormality and deformity, the presence of a similar substance to that which expands the melanophores of the frog and the pigment cells of some fish, in the blood and urine of the patients, and the presence of headache, hyperthermia, hypogenitalism, hypercholesterolaemia associated with obesity, diminished glucose tolerance, disturbance of the water-salt metabolism, lymphocytosis, and diminished vitamin C excretion. Of the 11 patients, 9 at one time or another showed the presence of the melanophore dispersion substance, and in the blood in 6 out of 7 cases tested: 4 cases tested gave negative reactions in the cerebrospinal fluid; hypogenitalism was present in 5, obesity with a raised blood cholesterol, constant mild hyperthermia in 3, and diminished glucose tolerance in 3. The associated abnormalities fall into two groups: (1) comprising the Laurence-Moon-Biedl syndrome and its variations, showing different degrees of degeneration involving the region developed in common with the optic vesicle, and (2) deaf-mutism and other apparatus of sensory reception.

Treatment

By atropine sulphate.—W. M. Brown treated 6 cases of retinitis pigmentosa with retrobulbar injections of a 1:1,000 solution of atropine sulphate. The patients were all in the third and fourth decades of life, and none had any syphilitic stigmas. The injections were given into the muscular cone twice weekly. Two years after the treatment there was definite improvement in 2 cases, in 1 the condition was apparently stationary, and 3 were not improved.

Tumours*Angiomatosis retinae*

Treated by catholysis and surface diathermy.—H. Kaye reports 2 cases of angiomatosis retinae in a brother and sister treated by Stallard's method of the combination of catholysis and surface diathermy. The author maintained contact with the patients for 12 months, and found that the treatment gave a completely satisfactory result, with full preservation of vision. The brother's eye had been protected from a certain retinal detachment, and the sister had been saved from threatened blindness.

Detachment*Aetiology*

A. Hagedoorn states that the white retinal striae which occur after detachment of the retinae are the result of a primary streak-like degeneration and proliferation of retinal tissue. The peculiar line-like arrangement of the retinal process may be due to the continuous folding and bending of the retina along this line in the period of detachment. This prolonged trauma may cause a linear degeneration of the retina, stimulating the activity of glial tissue.

Treatment

Surgical procedure.—W. L. Benedict summarizes his experience of surgical procedures for the cure of retinal detachment. In many cases the cause cannot be found, but in more than 90 per cent a rent in the retina or disinsertion is present. As surgical treatment is the only form of any value there is a temptation to employ it in unsuitable cases; Benedict and his colleagues have operated on a number of such cases, about 45 per cent of more than 100 operations being fairly successful.

E. C. Zorab reports an unusual case of detachment of the retina successfully treated by operation. The main features of the case were the large size of the tear which involved more than half the circumference of the retina; the folding in half of the detached retina so that its posterior surface was facing anteriorly; the replacement of the retina by ordinary operation, assisted perhaps by gravity, but not by retinal hooks or other devices; the great degree of recovery of vision after complete and wide separation of the macula for more than a week.

Benedict, W. L. (1941) *Proc. Mayo Clin.*, **16**, 140.

Brown, W. M. (1941) *Arch. Ophthalm.*, N.Y., **25**, 819.

Dax, E. C. (1940) *Quart. J. Med. N.S.*, **9**, 263.

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Kaye, H. (1941) *Arch. Ophthalm.*, N.Y., **25**, 443.

O'Brien, C. S., and Allen, J. H. (1940) *Arch. Ophthalm.*, N.Y., **24**, 742.

Rea, R. L. (1941) *Arch. Ophthalm.*, N.Y., **25**, 548.

Zorab, E. C. (1941) *Brit. J. Ophthalm.*, **25**, 229.

RHEUMATIC INFECTION, ACUTE

See also B.E.M.P., Vol. X, p. 639; Surveys and Abstracts 1939, pp. 135 and 523; 1940, p. 510; and p. 49 of this volume.

Bacteriology and Morbid Anatomy*Cardiac lesions*

Recovery of haemolytic streptococci.—S. Thomson and J. Innes, in the attempt to recover a haemolytic streptococcus from the cardiac lesions of acute rheumatism, examined at necropsy the heart in 10 cases of the disease. They obtained haemolytic streptococci from 5 out of the 10 cases. Successful culture was made from 11 valves out of a total of 26 showing acute lesions. Haemolytic streptococci were isolated from damaged valves but not from undamaged valves. Ten control necropsies were carried out, but from none was a haemolytic streptococcus isolated, although from a heart valve in 3 cases there was obtained an α type streptococcus which was not isolated from the blood. The authors are inclined to support the view that the cardiac lesions in acute rheumatism are due to infection with haemolytic streptococci.

Clinical Picture*Juvenile type*

Recurrences in streptococcal upper respiratory infections.—Ann G. Kuttner and E. Krumwiede report their observations carried out for 3 years on the relations between streptococcal upper respiratory infections and rheumatic fever in children. They found that the incidence of rheumatic recurrences after 3 outbreaks of streptococcal respiratory infection varied from none to a high proportion of cases. Comparison of the epidemic strains did not show any significant differences to account for the variations in the incidence of these occurrences. The authors' findings suggest that the vulnerability of the rheumatic patient to the effect of streptococcal upper respiratory infections varies, and depends on factors which at present are not understood. There were not any recurrences in children who escaped streptococcal upper respiratory infections during the three periods.

Association with acute appendicitis in children

A. G. Langmann discusses symptoms of acute appendicitis accompanying rheumatic fever in children. Nineteen cases with a diagnosis of acute appendicitis were observed and the patients noted to be suffering from abdominal pain, nausea, vomiting, and muscular spasms, except in 2 cases. Ten underwent laparotomy; of these 4 only had acute appendicitis, and one normal appendix was removed after which straightforward rheumatic polyarthritis without

abdominal pain developed. The remaining 14 cases are described as those of rheumatic pseudo-appendicitis, indistinguishable by abdominal symptoms alone from true appendicitis. Diagnosis is made more difficult by the usual appearance of pseudo-appendicitis at the onset of rheumatic fever before the development of full rheumatic symptoms. Pains are diffuse and become localized in the right lower quadrant, but they decrease and tend to disappear in 2-6 days. Joint pains may then appear, or the two pains may be coexistent. In 2 cases the patients developed acute appendicitis in the late stages of rheumatic fever. These were diagnosed as normal acute appendicitis superimposed on rheumatism. This was confirmed at operation when a pathological condition of the appendix not specifically rheumatic was observed. In acute appendicitis erythrocyte sedimentation is normal, unless perforation has occurred, but in pseudo-appendicitis the rate is high. This helps in diagnosis, but the possible case of concurrent appendicitis and rheumatic fever must be remembered and laparotomy performed if there is any doubt. The causes of pseudo-appendicitis are not known. Cases of abdominal lesions accompanying rheumatic fever have been reported, but they are not confirmed by the author.

Diagnosis

Two-step test

L. Kuskin and L. Brockman made 100 examinations on 38 ambulatory patients with rheumatic heart disease. Each examination included a sedimentation rate and a two-step test for the purpose of comparing the results of each in an evaluation of rheumatic activity. No relationship was found to exist between the ability to perform a normal two-step test and the extent of cardiac damage. Rheumatic activity was the major factor in reducing the exercise tolerance. In the clinically active group there were more abnormal two-step tests than rapid sedimentation rates. In the clinically inactive group the two-step tests were abnormal in a higher percentage of cases than the sedimentation rates.

Treatment

Prophylaxis

Sulphanilamide.—C. B. Thomas, R. France, and F. Reichsman gave sulphanilamide continuously to 55 patients with a recent history of acute rheumatic fever during 79 person-seasons. Sixty-seven patients with a similar history, but not given any such prophylactic treatment, were observed simultaneously during 150 person-seasons. The drug was taken from November to the end of June, generally in a dose of 1.2 grammes (20 grains) daily. No serious toxic effects were noted. Pharyngeal cultures, positive for the haemolytic streptococcus, were less numerous among the treated patients than among controls. While taking the drug none of the patients had a major attack of acute rheumatic fever or an acute haemolytic streptococcal infection. Among the controls 15 major attacks of rheumatic fever occurred, and in 2 subacute bacterial endocarditis supervened.

Kuskin, L., and Brockman, L. (1940) *Arch. Pediat.*, **57**, 578.

Kuttner, Ann G., and Krumwiede, E. (1941) *J. clin. Invest.*, **20**, 273.

Langmann, A. G. (1941) *J. Pediat.*, **18**, 599.

Thomas, C. B., France, R., and Reichsman, F. (1941) *J. Amer. med. Ass.*, **116**, 551.

Thomson, S., and Innes, J. (1940) *Brit. med. J.*, **2**, 733.

SCARLET FEVER

See also B.E.M.P., Vol. XI, p. 1; Cumulative Supplement, Key No. 1387; Surveys and Abstracts 1939, pp. 77 and 525; 1940, p. 513; and p. 67 of this volume.

Complications, Sequelae, and Associated Diseases

Gangrene of feet

A. L. Hoyne and L. Smollar record gangrene of both feet in a male child, aged 4 years, as a complication appearing on the twenty-third day of scarlet fever. The condition was ascribed to the wide-spread inflammation of the small arteries. This complication is very rare; during 28 years about 30,000 cases of scarlet fever have been admitted to the Cook County Contagious Disease Hospital, and this is the second example of gangrene. The authors collected references to 17 previously published cases, of which 16 were of dry gangrene; in 5 both feet were involved. One case only proved fatal—that of a boy, aged 5 years, with gangrene of all four extremities, both cheeks and both ears, recorded by A. L. Hoyne in 1915. Four days after the onset of gangrene a surgeon was called in and advised immediate amputation through the right thigh and probably a similar procedure on the left side. Nevertheless radical surgical treatment was postponed and final amputation was delayed for 3 months. Emphasis is laid on the inadvisability of early surgical intervention on gangrene in scarlet fever.

Treatment

Immunization

Toxin in tablet form.—G. F. Dick and Gladys H. Dick describe the preparation of toxin suitable for oral immunization against scarlet fever. This was supplied in the form of enteric-coated tablets and employed to immunize 131 susceptibles to scarlet fever. Preliminary skin tests were made in every case, and these were repeated two weeks after completion of the immunization. The tablets were taken immediately after meals, beginning in most cases with 100,000 skin-test doses and increasing to 6 or 10 million skin-test doses a day for the last

3 to 6 days. Of 102 persons who completed the immunization, 94.7 per cent were found to be immune on retesting.

Dick, G. F., and Dick, Gladys H. (1940) *J. Amer. med. Ass.*, **115**, 2155.

Hoeyne, A. L. (1915) *J. Amer. med. Ass.*, **45**, 1725.

— and Smollar, L. (1941) *J. Pediat.*, **18**, 242.

SCLERODERMIA

See also B.E.M.P., Vol. XI, p. 37; Cumulative Supplement, Key No. 1390; and Surveys and Abstracts 1939, p. 527; 1940, p. 516.

Definition

Relation of progressive scleroderma to dermato-myositis

Common features.—According to G. B. Dowling progressive scleroderma and dermato-myositis are the same disease. The condition has certain characteristics in common with thyrotoxicosis, viz. the skeletal muscles show similar pathological alteration in progressive scleroderma and thyrotoxicosis; clinically the muscular symptoms of myopathic scleroderma, dermato-myositis and thyrotoxic myopathy are identical; creatinuria occurs in toxic, and in many cases of non-toxic goitre, and in progressive scleroderma; some disturbances in carbohydrate metabolism in thyroid disease have their counterparts in scleroderma, and calcium metabolism is affected in both; in 19 reports of necropsies on cases of progressive scleroderma, in which the thyroid was examined histologically, morbid changes in the thyroid were described in all. Changes were also present in 2 of the author's cases. These facts are regarded as suggesting an aetiological relation between the conditions.

Dowling, G. B. (1940) *Brit. J. Derm.*, **52**, 242.

SCURVY

See also B.E.M.P., Vol. XI, p. 44; Cumulative Supplement, Key No. 1391; Surveys and Abstracts 1939, p. 528; 1940, p. 517; and pp. 5, 13, and 49 of this volume.

Clinical Picture

In an infant

W. Levy, N. M. Greenstein, and S. R. Berenberg report an atypical case of infantile scurvy in an infant aged 4 months. The child who had been breast-fed for 2 months, and afterwards on cow's milk, was in an excellent state of nutrition yet apparently failed to absorb vitamin C. The distribution of oedema was more wide-spread than usual, and it occurred on the face, forehead, and upper extremities. On palpation the subcutaneous tissues had a bony consistency, but X-ray examination failed to disclose any formation of new bone. The cortices of all the long bones were particularly thickened, and encroached on the medullary space, in striking contrast to the thin cortex generally found in scurvy. With healing of the scorbutic process, as a result of treatment, there was an irregular calcification in the sub-periosteal region. In this case there was an adequate vitamin C intake.

Levy, W., Greenstein, N. M., and Berenberg, S. R. (1941) *Arch. Pediat.*, **58**, 168.

SENESCENCE AND SENILITY

See also B.E.M.P., Vol. XI, p. 69; and Surveys and Abstracts 1939, p. 528; 1940, p. 518.

Normal Old Age

Care of the aged poor

J. C. C. Langford pleads for a scheme whereby help can be given to the impecunious old who have greater capacity for mental pain than infants who inspire much more interest and help. It is suggested that each old person or old couple should have at least two private rooms, one for sleeping in and one for sitting in, or flatlets in blocks in healthy localities with a resident nurse and communal kitchen to each block, and that an attempt should be made to provide all the advantages of a well-run institution with as little of the institutional atmosphere as possible. It is realized that at the present time of emergency this kindly suggestion is for consideration when the days of peace come.

Longevity

Sex and profession as influential factors.—In his twenty-sixth annual analysis of longevity recorded in *The Times*, C. B. Gabb supplies information of what occurs amongst those in a presumably fair financial position in life. During 1940 the front pages of *The Times* recorded the deaths of 438 persons of 90 or more years of age, as compared with 411, the average for the previous 25 years, the extremes being 531 in 1938 and 283 in 1918. Of the 438 deaths 302 were of women, 210 being married, 26 widows of clergymen; there were 136 men, 15 being in Holy Orders, thus confirming the general opinion that women are longer-lived than men, and the clergy surpass other professions in this respect. Of the men the most distinguished was General Sir Bindon Blood, born in 1842. Herbert Jenner-Fust, the oldest Etonian, was an example of the heredity of longevity, for his father, like him, lived to within two years of his century. The front pages of *The Times* recorded 12 centenarians as compared with an average of 9 during the previous 25 years. In an article on analysis of physique J. I. Cohen agrees that there is a clear relation between physical build and longevity. At the younger ages those who are underweight or markedly underweight show a high mortality. At the older ages some degree of overweight is an asset. In general, mortality seems to rise with increase

in weight above the optimum. It also rises with an increase in the excess of abdominal over chest girth (Dublin and Lotka).

Pathological Old Age

Surgery of the aged

Operative risks.—On the basis of an analysis of 536 patients who underwent major operations in the Winnipeg General Hospital during the years 1931–8, and on personal experience, A. W. S. Hay insists that individuals may be chronologically more than 70 and yet physically much younger, that a 10 to 30 per cent mortality risk is much less to be dreaded by an old man than months or possibly years of misery, and that the problem of surgery for the aged will become progressively more important with the increasing prolongation of life due to advances of medical science. In advanced age some operations should be avoided, namely, plastic operations and those to relieve minor discomforts, such as those for bunions, and herniotomy for herniae controlled by a truss. Operation should be recommended in (1) emergencies, to save life from imminent danger, (2) to relieve severe and recurrent pain, e.g. biliary colic, and to overcome physical disability (large herniae), and (3) malignant disease. Statistics are quoted to show that the risk is not nearly so great as might be expected: among 100 major operations on patients generally over 70, Nelson reported 8 operative deaths, 2 of which were largely, and probably entirely, attributable to the medical attendant's opposition to operation. Smith, as long ago as 1907, reported a mortality of 12.6 per cent. At the Winnipeg Hospital the rate was 16.6 per cent, or roughly three times as high as would be expected in younger patients. Among operations on cases of benign hypertrophy of the prostate in men over 70 the total mortality was 13 per cent, being 7.7 per cent for the punch operation, or twice as high as the average; for suprapubic prostatectomy it was 24 per cent, or about treble that in younger men, and due to heart or lung, and urinary infection before operation. Among the causes of death in the 536 cases, pneumonia was responsible ten times as often as would be expected in younger subjects. In 1 per cent pulmonary embolism was the cause of death; the incidence of post-operative pulmonary embolism runs roughly parallel with age, and it is therefore important to prevent thrombosis by muscular exercise after operation, and possibly by the use of heparin. Since 90 per cent of post-operative lung complications begin as atelectasis, it is essential to ensure complete ventilation of the lungs. To prevent faecal impaction, common in the aged, an occasional rectal examination is advisable.

The following conclusions are drawn: (1) an individual's chronological age must not be accepted as a criterion of survival of an operation, (2) age is only one factor in the estimation of the surgical risk, (3) intravenous treatment must be cautiously undertaken on account of arteriosclerosis, myocardial degeneration, and liability to pulmonary oedema, (4) vaccines before operation have a definite value in diminishing chest complications and peritonitis, (5) sedatives and hypnotics should not be given as a routine before operation, but with individual consideration, (6) a relatively prolonged pre-operative period of preparation is advisable before a major operation is performed on elderly patients.

Diseases in Old Age

Acute rheumatic fever

H. L. Rakov and J. S. Taylor report a case of acute rheumatic fever, in a woman aged 61, with extensive acute rheumatic myocarditis, which caused her death after extraordinarily confusing clinical manifestations. The chief clinical features were attacks of paroxysmal nocturnal dyspnoea associated with congestive heart failure. The absence of considerable cardiac hypertrophy, significant valvular inadequacy, and of hypertension indicated that the heart failure was due solely to the active myocardial inflammation. The necropsy showed a large number of huge Aschoff bodies which had destroyed extensive areas of cardiac muscle, swelling of the intact muscle fibres, and acute rheumatic lesions, swollen endothelial cells and oedema of the walls of the small coronary branches which in a few places were completely occluded. The adventitia showed cellular infiltration.

Diseases Specially Prone to Occur in Old Age

Gastro-intestinal symptoms

J. Meyer and H. Necheles point out that, although gastro-intestinal symptoms are common in old age, gastro-intestinal disease is relatively uncommon. Old people show changes in the salivary, gastric, and pancreatic secretions, except amylase, in the form of a decrease in the quantity of secretion and enzymes. This diminution in the quantity of secretion apparently does not affect intestinal digestion. In spite of the diminution in the secretion, the secretory mechanism is capable of response under adequate stimulation. The restrictions imposed on old people because of fear of inadequate digestion of carbohydrate, protein, and fat do not appear to be warranted. Acute peptic ulcer with severe complications occurs in old people in association with cardiac, renal, hepatic, and prostatic disease.

Syphilitic infection

Incidence.—From serological and other observations carried out at the Tooting Bec hospital (2,300 beds), the only hospital in Great Britain entirely devoted to the care of senile demented, L. T. Hilliard and B. H. Kirman conclude that syphilitic infection is not absolutely incompatible with advanced age, and instance a woman aged a hundred years with a strongly positive blood-Wassermann reaction. The longest incubation period of syphilis is stated to

be fifty years (W. D. Nicol and Effie L. Hutton). That the prognosis is better in untreated than in inadequately treated patients is accepted by Hilliard and Kirman, who point out difficulties in the diagnosis in the aged by physical signs: thus pupillary abnormalities (inequalities, irregularities, and inactivities to light) are extremely common in senile patients, as are also absence of abdominal reflexes, and the presence of extensor plantar responses.

Senile osteoporosis of the spine

J. R. Black reports on the 208 cases of senile osteoporosis of the spine in which radiological examination was available at the Mayo Clinic. It is defined as a crippling disease of old people, with severe backache and progressive spinal deformity, and extreme decalcification of unknown aetiology. Though relatively common, it has only recently been recognized as responsible for severe pain in the back. There were 167 women and 41 men, and the average age at which the diagnosis was first made was 62, the extremes being 45 and 87 years. The vertebral bodies show very few trabeculae and collapse, the intervertebral disks becoming expanded. Although extreme osteoporosis may be present without symptoms, a fairly consistent clinical picture is seen in the following case of a woman aged about 59 years, with a feeling of weakness, fatigue, or dull ache in the lower part of the back which gradually got worse and could be felt in any part of the back. This is the early stage and lasts about 3 years. Then after a jar, a twist, a fall, on lifting a weight or bending, the patients may feel a sudden snap or acute pain which may confine them to bed for several days or weeks. The course is usually progressive with intermittent attacks of sharp pain and in the intervals dull persistent backache. Pain is often referred to the front of the chest, abdomen, or the lower limbs. There is often mental depression, and there is usually a thoracic kyphosis with increased cervical lordosis. This clinical picture may be present in other diseases of the spine, as in spondylitis, fractures, malignant metastases, and in toxic goitre, hyperparathyroidism, and myeloma. The radiological appearances are of characteristic expanded disks. Treatment has been directed to the correction of calcium and phosphorus deficiency in the bone, to prevention or correction of the deformity, though more can be done for prevention, by high backed corsets, than for correction. Relief of pain should be sought by rest, recumbency, a spinal support, heat and massage in the acute phases, and sedatives.

T. H. Howell, from experience at the Royal Hospital, Chelsea, with its 400 pensioners, contests any suggestion that 'rheumatism' is an inevitable accompaniment of old age. During the year October 10, 1939, to October 10, 1940, there were among the 400 pensioners 47, or 11.4 per cent, attending the Rheumatic Clinic, 24 of these being the subjects of fibrositis, and 6 of osteoarthritis. The circumstances of the pensioners are favourable as they are free from anxiety, provided with ample diet, adequate vitamins, and a warm uniform. Ten patients, all over 70 years of age and 2 over 80, were treated for fibrositis, far the most successful method being Scott's dressing well rubbed in under the heat from an infra-red lamp, and the excess wiped off.

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SEX HORMONES

See also B.E.M.P., Vol. XI, p. 90; Cumulative Supplement, Key Nos. 1396-1398; Surveys and Abstracts 1939, pp. 17, 34, 108, and 531; 1940, pp. 20, 21, 55, 131, and 520; and pp. 4, 20, and 81 of this volume.

Source and Constitution

Hepatotropic and cardiotropic properties of sex hormones

V. Korenchevsky, K. Hall, R. C. Burbank, and J. Cohen summarize the results of work on the numerous effects produced by sex hormones on organs other than those of sex, as shown by changes in weight of the organs in gonadectomized rats in comparison with those of normal intact animals, and the changes in weight of the organs of rats injected with various sex hormones as compared with those of uninjected litter-mates. The histological changes in some of the non-sex organs of the rats found by the authors, in their published and unpublished experiments, have been brought forward, and the knowledge of the subject reviewed in the case of the adrenals of males and females, livers of males, and kidneys of both sexes. In this article experiments made with sex hormones on 281 male and 503 female rats are recorded with the resulting effects on the weights and histological structure of the liver and heart, and also on the isolated heart of 46 male rats. Hepatotropic and cardiotropic properties are non-sexual effects of male hormones, especially of androsterone and testosterone propionate. Gonadectomy in males exerts a depressing effect on the development of the liver

and to a less extent on the weight of the heart in males, but has less effect in females. In experiments on females special attention was paid to two male hormones, androsterone and trans-dehydroandrosterone. It is suggested that androsterone is preferable to the testosterone esters as a physiological stimulant to the liver, heart, and kidneys in both sexes since it produces a weak effect only on the male and female sex organs; it is most inadvisable to stimulate the sex function in patients with serious disease of the liver, heart, and kidneys. In view of the toxicity of large doses of oestrogens, great caution should be exerted in their clinical use, but it is possible that small doses of some oestradiol esters, such as oestradiol benzoate-butyrate, with a prolonged and mild action given with long intervals between the injections may be considered to stimulate the liver and perhaps other organs.

Excretion of sex hormones in children

Tests made at various ages in boys and girls.—I. T. Nathanson, L. E. Towne, and J. C. Aub describe their observations to determine quantitatively the excretion of sex hormones in normal children. Between the ages of 3 and 7 the amount of androgens and oestrogens excreted is small and the same in both sexes. There is an increase between the ages of 8 and 11 with a predominance of androgens in boys and oestrogens in girls. About one and a half years before commencement of menstruation oestrogen excretion increases rapidly and becomes cyclic. There are not cycles in the excretions of boys, nor in the androgen excretions of either sex. The onset of secondary sexual characters in boys is accompanied by a sudden increase in androgen excretion. The follicle-stimulating pituitary hormone appears in the eleventh year in girls and between the twelfth and thirteenth year in boys. With a better technique it could probably be detected sooner.

Anterior pituitary hormones

Thyroidotrophic hormone.—J. Fraenkel-Conrat, H. Fraenkel-Conrat, Miriam E. Simpson, and H. M. Evans report the results of an investigation into the purification of the thyroidotrophic hormone from other pituitary hormones, such as the lactogenic, the growth, adreno-corticotrophic, and gonadotrophic. Although the biological properties have been amply studied, it is surprising that only a few attempts have been made to purify and free this hormone from other active components. The authors employed a method, described as relatively simple, which constantly gave good results. The anterior pituitary protein associated with thyrotrophic activity is relatively soluble in distilled water and easily soluble in dilute salt, acid, or alkaline solutions. It contains 13 per cent of nitrogen, 3.5 per cent of carbohydrate, and 2.5 per cent of glucosamine; treatment by cystine under favourable conditions inactivates it, ketone treatment for five minutes at 22° C. in acetate buffer of a hydrogen ion concentration of 5.6 causes considerable loss of activity. It contains about 10 per cent of the interstitial cell-stimulating hormone, but very little lactogenic, adreno-corticotrophic, growth-stimulating or follicle-stimulating hormones. The final product represents a hundred-fold purification with recovery of about one-third of the total thyrotrophic activity of the original material.

Ovarian follicle-stimulating hormone.—H. Fraenkel-Conrat, Miriam E. Simpson, and H. M. Evans describe a method for the preparation from the sheep's anterior pituitary of a highly purified protein with a specific stimulating effect on ovarian follicular development (F.S.H.), with a fourfold increase in potency. The protein representing this hormone contains 13 per cent of nitrogen, is readily soluble in water and, in the absence of electrolytes, in 50 per cent acetone and in 70 per cent alcohol. It is quite stable, and can be obtained as a dry powder. Preliminary experiments on its solubility in different concentrations of ammonium sulphate indicate that it is mainly a single protein.

Relation to blood pressure

Effects of progynon and perandren.—A. Guiridham describes 2 cases to illustrate the relation of oestradiol and testosterone to blood pressure. The first patient, a woman of 78, with a blood pressure of 220/120, was acutely depressed, had gross arterial degeneration, and enlargement of the left ventricle. Progynon (oestradiol) ointment, 0.14 milligram, was rubbed into the skin daily. A fall of blood pressure to 150/70 was attained in a fortnight and remained stable after suspension of treatment. The second patient, a woman of 53, with melancholia, arteriosclerosis, and a degenerate myocardium, had a blood pressure of 164/84. Progynon ointment (0.28 milligram) was rubbed in daily and the amount doubled 2 weeks later. After 31 days of varying doses the blood pressure dropped to 96/60, the blood pressure during that period fluctuating in direct relation to the increases or decreases in the dosage. A week of perandren (testosterone) treatment (2 milligrams daily) raised the blood pressure from 108/60 to 130/70 and to 148/70 with a double dose. Reduction in the blood pressure of psychoneurotic females by oestradiol treatment has had beneficial results. Although the relation between sex hormones and blood pressure is obvious, definite conclusions cannot yet be drawn.

Ovarian hormones and synthetic oestrogenic substances

Action of oestrogens on the pituitary and pancreas.—It has been shown by W. Cramer and E. S. Horning (1936) at the Imperial Cancer Research Fund Laboratories that by the prolonged action of oestrogenic substances the pituitaries of mice undergo hypoplasia and that this is followed by enlargement of the islands of Langerhans. E. Vazquer-Lopes, working in the same laboratories, has examined the pituitaries and pancreases of a number of mice which had for several months been treated by oestrogenic substances. Many pituitaries

showed enlargement, haemorrhages, and cytological evidence of over-activity. It was also found that all the cells of the islet tissue showed hypertrophy of the Golgi apparatus of a degree never seen in normal mice. The cells were much enlarged and some showed two or three nuclei. The presence of giant islands with or without acinar residues and the apparent formation of new minute islets is not an absolute proof of a real increase of the endocrine portion of the pancreas, but the histological architectural alteration seems to be the result of proliferation of the insular cells.

Effect on lactation.—S. J. Folley states that apart from their well-known inhibitory effect on lactation, oestrogens can exert a galactopoietic action which is shown chiefly by an increase in the concentration of both fatty and non-fatty solids in the milk. The threshold for this enrichment effect is lower than for inhibition. Small doses generally cause enrichment, whereas large doses also elicit inhibition. The two effects appear to be more readily separable with natural oestrogens than with diethylstilboestrol. It is argued that oestrogenic hormones and some other substances can stimulate not only mammary development but, when given in small doses, also lactation; they can inhibit both in large doses.

Prevention of fibromyomas after oestrogen injections

Desoxycorticosterone.—A. Lipschütz and L. Vargas, Jun. report experiments designed to prevent uterine and extra-genital fibromyomas produced by prolonged injections of oestrogen. Two groups of guinea-pigs were injected with oestradiol, one group receiving in addition a simultaneous injection of testosterone or progesterone. Uterine fibromyomas were completely prevented when the testosterone or progesterone were used in the proportion of 50:1 and 150:1 respectively to the quantity of oestradiol injected. Implanted subcutaneously in tablets the proportion required was, 13:1 for progesterone. Thus subcutaneous technique is the most economical way of preventing fibromyomas by oestrogens. As, however, testosterone and progesterone exert a masculinizing action and affect the uterine mucosa, the use of cortical hormones was considered; the acetic ester of synthetic desoxycorticosterone was used, being the cortical hormone most similar to progesterone. Again, experiments were carried out as above, the first group receiving oestradiol only and the second oestradiol and desoxycorticosterone. The first group showed persistent vaginal opening, genital bleeding, ulceration of the labia, uterine and extra-genital fibromyomas, high incidence of the tumours, great development of the uterus, and purulent peritonitis. The second group did not show any of these tendencies except temporary opening of the vagina. The hormone had not any masculinizing effect, and the proportion required was about 3:1 to oestradiol. The effect on the uterine mucosa has not been examined microscopically. The synthetic cortical hormone is thought to be superior to testosterone or progesterone in the prevention of tumours and toxic effects, but quantitative proof is needed. Esters of testosterone and other synthetic androgens have been tried and the results will be reported later.

Stilboestrol in early pregnancy.—H. O. Burdick and H. Vedder found that stilboestrol can, in common with other oestrogens, modify the passage of fertilized ova through the oviducts of mice. Subcutaneous injections of one milligram dissolved in sesame oil cause an acceleration of the rate of tubal passage, whereas injections of 0.005 milligram result in the tubelocking of the ova. Pregnancy is interrupted with both dosages. Stilboestrol apparently has a toxic effect on the ova, and on the corpora lutea of early pregnancy.

Alleged hepatotoxic effect of stilboestrol.—S. C. Freed, E. E. Rosenbaum, and S. Soskin found that the administration of one milligram of stilboestrol daily did not exert any toxic action on the livers of a group of menopausal women examined. This was true even when doses of 5 to 10 milligrams were given, or in the case of women who, as judged by the bromsulphthalein retention test, showed some hepatic dysfunction at the beginning of treatment. Moreover, relatively huge doses of stilboestrol did not produce gross or cellular pathological changes in the liver or kidneys of rats or of a dog. A patient with definite hepatic damage who was recovering from an attack of acute hepatitis was able to take 10 times the usual therapeutic dose of stilboestrol for 3 weeks without the slightest evidence that his convalescence had been impeded. The authors conclude that stilboestrol is not significantly toxic to the liver.

Stilboestrol as cause of gynæcomastia in a male.—C. W. Dunn found that the administration of 400 milligrams of stilboestrol to a man of 27 was followed by prominent bilateral gynæcomastia, the physical characteristics of which were dissimilar to those observed in males treated with natural oestrogenic substances. It also markedly reduced sexual activity from a hypersexual to what was considered a hyposexual state. It was assumed that the therapeutic results observed were due directly to depression of the anterior pituitary gonadotrophic function and indirectly to inhibition of male hormone production in the testes or primary depression of testicular hormone formation. None of the toxic effects attributed to stilboestrol was noted.

Use of endometrial extract.—D. R. Mishell and L. Motyloff report that removal of the uterus in the rabbit produces changes in the ovary which can be demonstrated within 3 months of the operation. These changes consist of a precocious atrophy of the follicular apparatus, abnormalities in the growth of the follicles, atypical development and degeneration of the corpora lutea, and compensatory hypertrophy in the interstitial gland terminating in cellular degeneration. These changes are modified by the administration of endometrial extract prepared from cow's endometrium which seems to regulate the process of follicular proliferation, protect the functional elements of the ovary, and retard the process of atrophy.

Synergism of oestrogens with pituitary gonadotrophins.—Miriam E. Simpson, H. M. Evans, H. L. Fraenkel-Conrat, and C. H. Li confirm the observation of R. I. Pencharz that the ovaries of hypophysectomized rats show increased size, due to enlargement of the follicles as the result of the combined action of stilboestrol and chorionic gonadotrophin. They also obtained evidence of a similar synergism when hypophysectomized rats were given stilboestrol and the follicle-stimulating hormone (F.S.H.) of the anterior pituitary, but not with the interstitial cell-stimulating hormone (I.C.S.H.).

Effect of light on oestrous cycle in cats.—A. B. Dawson investigated experimentally the effect of increased illumination on the anoestrous period in cats. Seven cats, whose normal breeding season was from mid-January to mid-July, were subjected in October to gradually increasing periods of illumination under favourable physical conditions. Four of them exhibited early oestrus, the earliest after 49 days and the last after 62 days. In the following year 6 cats were subjected to decreased periods of light followed by increased periods. All 6 showed early oestrus, the first after 50 days from the time of increased lighting and the last after 71 days. Recent suggestions that increased illumination will not accelerate the onset of oestrus during or just before the breeding season, are not borne out by experiments performed in late December, when increased illumination periods induced early oestrus after intervals of from 37 days to 100 days. The response was probably conditioned by normal light increments received up to the last day of December.

Male sex hormones

Rate of excretion of neutral ketosteroids (androgens).—N. B. Talbot, A. M. Butler, and E. A. MacLachlan estimated the rate of excretion of neutral ketosteroids by patients with male sexual precocity, virilism, or Cushing's syndrome, not associated with carcinoma of the adrenal cortex. They conclude that the β neutral ketosteroids arise solely from substances produced by the adrenal cortex; the rate of excretion of adrenal ketosteroids may therefore be an index of at least one aspect of adreno-cortical activity. The assay of the α , β , and total neutral ketosteroids gives specific information which may be useful in the differential diagnosis of adreno-cortical hyperplasia, Cushing's syndrome without adrenal tumour, and adreno-cortical carcinoma.

Effects of small doses on the sex organs of rats.—H. S. Rubinstein and A. A. Kurland, investigating the effect of testosterone propionate on the testis and accessory sex organs of rats, found that, in daily doses of 0.0025 milligram given subcutaneously for either 10 or 20 days, there was not any discernible effect. The administration of 0.0050 milligram for 10 days led to a 46.6 per cent increase in the weight of the seminal vesicle, and a 28.5 per cent increase in the weight of the prostate.

Use of Sex Hormones in Treatment of Menstrual and Climacteric Disorders

Mode of administration

Implantation of progesterone.—D. R. Mishell obtained satisfactory results from the implantation of pellets of progesterone in cases of habitual abortion, threatened abortion, and primary dysmenorrhoea. Of 4 cases of habitual and threatened abortion, 1 patient was delivered at full term, and at the time of the report 1 was in the eighth month, 1 in the third month, and 1 in the sixth month of pregnancy. Of 6 cases of dysmenorrhoea, relief of pain was obtained in 4. Of 4 cases of functional bleeding clinical cures were obtained in 2. The tablets implanted weighed from 45 to 60 milligrams.

Clinical Uses of Male Sex Hormone

Eunuchism and hypogonadism

Testosterone and testosterone propionate.—A. W. Spence treated 2 patients with eunuchism, and 4 with hypogonadism, by intramuscular injections of testosterone propionate, implantation of testosterone tablets, inunction of testosterone propionate as an ointment or tincture, inunction of testosterone as an ointment, or the oral administration of methyl testosterone. In all cases the treatment established potency and caused increased growth of the penis and scrotum, deepening of the voice, and gain in weight, and in 5 patients increased growth of hair on the face, body, and limbs. In several it removed psychological disturbances and improved the mental outlook; increased pugnacity, libido, muscular strength, and growth of the testes and prostate. In individual patients it hastened union of the epiphyses and caused normal development of the larynx, tenderness of the nipples, muscular hypertrophy, and oedema of the legs. The maintenance dose of testosterone propionate intramuscularly was 50 to 75 milligrams per week, in 2 or 3 injections. Daily inunction of testosterone propionate as an ointment was 32 to 49 milligrams per week, and of testosterone as an ointment 17.5 milligrams per week. Oral administration of methyl testosterone was 350 milligrams per week, in doses of 10 milligrams 5 times a day.

Testosterone propionate

Eunuchs.—A boy, 15½ years old, eunuchoid from the age of 5, was treated by I. Rapfogel with injections of testosterone propionate for 2 years. His height was 60½ inches and his weight 87½ pounds, and the 'bone age', as determined radiographically, was approximately 13 years. The ratios between upper and lower measurements, i.e. height above and below upper border of symphysis pubis, and between height and arm span showed that the long bones were relatively longer than normal, as is usual in eunuchoidism. When the dosage of testosterone propionate had reached 30 milligrams weekly and had been maintained at this level for several

months, growth was markedly stimulated, with a progress towards the normal height and weight and in the ratio between long and short bones. Prolonged androgenic therapy had no apparent effect on closure of epiphyses, judging by radiological evidence and by the stimulation of growth. During treatment the penis enlarged, hair developed in the pubic region, erections and emissions of seminal fluid occurred, and the patient's behaviour assumed a more masculine aspect.

Testosterone.—E. Simonson, W. M. Kearns, and N. Enzer report on the results of testosterone therapy on 4 male patients (2 eunuchoids and 2 castrates) for 4 weeks. There was an increase of muscular efficiency and the absolute muscular strength was slightly increased. The maximal increase of pulse rate during dynamic work was diminished, indicating a more efficient circulatory system. The pulmonary ventilation was slightly decreased in static work and unchanged in dynamic work. The fusion frequency of flicker was increased, thus pointing to an increased resistance of the central nervous system to fatigue.

Methyl testosterone given orally.—Rita S. Finkler and G. M. Cohn employed methyl testosterone by mouth in a male castrate. The patient had previously been receiving intramuscular injections of testosterone, but these were discontinued because of the discomfort caused by persistent erections. It was found that a daily dosage of 75 milligrams of methyl testosterone by mouth, divided into three doses at 6-hourly intervals, controlled headaches, crying spells, gain in weight, despondency, and loss of libido. The external genitalia increased in size, and the metabolic rate rose from minus 14 per cent to plus 6 per cent.

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SEXUAL BEHAVIOUR AND ABNORMALITIES

See also B.E.M.P., Vol. XI, p. 110; and Surveys and Abstracts 1940, pp. 60 and 527.

Perversions and Inhibitions

Homosexuality and lesbianism

Leptazol therapy.—N. M. Owensby assumes that homosexuality and lesbianism are symptoms of an underdeveloped schizophrenia which has been arrested at the particular phase in its psychosexual development when the libido became fixed, and that leptazol (cardiazol, metrazol) liberates this previous fixation of the libido so that the psychosexual energy becomes free once more to flow through regular physiological channels. He therefore employed the drug in 5 cases of homosexuality and 1 of lesbianism. The homosexual patients received from 6 to 15 leptazol shocks, and in all cases the homosexual tendencies disappeared, and had not been observed for periods of from 3 to 18 months. The woman, aged 23, said to have been a lesbian since puberty, received 10 leptazol shocks, and later became infatuated with a hospital intern. It is suggested that further work on this subject should be done.

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SHOCK AND COLLAPSE

See also B.E.M.P., Vol. XI, p. 126; Cumulative Supplement, Key No. 1400; Surveys and Abstracts 1939, p. 537; 1940, pp. 11 and 527; and pp. 1, 8, and 38 of this volume.

Definitions and Aetiology

Thrombocytopenia in traumatic shock

Effect of splenectomy.—A. Aihlein and D. B. Kendrick, Jun. investigated experimentally the number of thrombocytes in the blood during traumatic shock induced by injury of the small intestine in 6 dogs, 3 of which were splenectomized. There was a very gradual but definite diminution in the number of thrombocytes in the arterial and venous blood of the femoral vessels as shock developed. The thrombocytopenia was the same in the splenectomized and non-splenectomized dogs; but was less pronounced than in anaphylactic shock, in which the thrombocytopenia has been ascribed to destruction and pooling of the thrombocytes. Aihlein and Kendrick's experiments militate against the view that the spleen plays any part in the thrombocytopenia of traumatic shock.

Hypotheses of Shock

Fat-embolism

Associated with injury.—R. A. Rowlands and C. P. G. Wakeley record 3 cases (2 with necropsies) of fat-embolism and review the subject which had attracted considerable attention from physiologists, such as Richard Lower (1669), Magendie (1821), and E. Wagner, the pathologist, who in 1862 collected 48 cases, 15 of which were associated with compound fractures, 12 from acute suppuration, and 15 from severe injury of bone or soft parts. It received little attention, however. It is said to be eight times more frequent in males than in females, in correspondence with the incidence of injury. As the main clinical forms, the pulmonary, systemic, and cardiac have been described; but often, as in the 3 cases reported, the clinical picture indicates both pulmonary and systemic infarction. But 2 clinical forms of pulmonary and 3 of cerebral fat-embolism have been described by Groendahl and by Vance respectively. There is usually fever, but the temperature ranges from subnormal to 106° or 107° F. Tachycardia is constant, the skin and mucous membranes often showing petechial haemorrhages at the time of the onset of stupor; the blood and the urine have been found to contain fat, and dyspnoea with crepitations over the lungs, followed by restlessness, insomnia, delirium, and coma make up the clinical picture. The differential diagnosis should be made from delirium tremens, various cerebral lesions, septicaemia, broncho-pneumonia, pulmonary embolism, and blast lung (pulmonary concussion). Treatment is mainly prophylactic, namely, avoidance of unnecessary movement of fractures, and palliative. Saponification and emulsification of the fat is still in the experimental stage. Administration of oxygen is recommended.

Role of adrenal secretions

Histamine-like substance.—Two papers on shock were read before the Canadian Medical Association in June 1940. Under the title 'Studies in Experimental Shock' C. H. Best and D. Y. Solandt define shock 'when fully developed' as 'characterized by low blood pressure, due probably to deficient return of blood to the heart. There is little or no real concentration of the blood, but there is a marked increase in the cellular elements, indicating a loss of plasma but not of cells from the blood stream.' The essential feature of advanced shock is the low blood pressure; the speed with which this develops depends chiefly on the method used for producing the shock. Thus in histamine administration true shock develops in a few minutes and may continue long after the action of histamine has ceased; the speed of the onset after haemorrhage depends chiefly on the amount of blood removed; shock due to trauma and injury occurs after a limb is grossly damaged, and shock due to injury and pulping of muscles occurs in 4-24 hours. J. C. Meakins in a general article on 'Shock—Its Causes and Treatment' points out that, although it has been regarded as a peril of surgical practice, it occurs in other conditions, such as peripheral circulatory failure, as distinguished from congestive circulatory failure, severe infections, anaemia (haemorrhagic or otherwise), pancreatitis, peritonitis, burns, acute coronary and pulmonary artery lesions, high intestinal obstruction, cholera, and dysentery. The classical descriptions of shock emphasize the fall of blood pressure, but this is one feature only and a late one; the first symptoms are unusual weakness and restlessness, followed by a rapid and a small pulse volume, the blood pressure being well sustained or even raised. The present position about the causation of shock is reviewed, stress being laid on the increased permeability of the capillaries and the consequent diffusion of plasma fluids into the surrounding tissue spaces. The following hypothesis is tentatively put forward: in normal conditions the adrenals secrete just enough cortin or similar substance for the needs of the body. Under the stimulus of insults it produces an excessive amount to meet protective requirements, the surplus being excreted in the urine. But if the insult is prolonged or very severe, the amount required for protection is greater than can be provided or utilized, and as a result histamine or a histamine-like substance is able to affect the capillary permeability so that plasma and cellular fluid migrate into the pericellular spaces, producing reduction of blood volume and 'cellular dehydration', especially of the intestine and lungs. The onset and progression of shock are regarded by Meakins as most certainly detected by frequent and accurate estimations of haemoglobin or by the haematocrit. A rising haemoglobin percentage or an increase of the cells to plasma ratio indicates haemo-concentration due to loss of plasma through the capillary walls.

Neurogenic hypothesis

Nervous factor in traumatic shock.—V. Lorber, H. Kabat, and E. J. Welte report that shock can be produced in the cat by appropriate trauma to a perfused hind limb separated com-

pletely from the general circulation, and communicating with the body only by means of its nerves. These experiments confirm the reality of a nervous factor in traumatic shock, though they do not explain the relative importance of this as compared with other causal factors.

Treatment

Surgical shock

Effect of heat and cold.—A. Blalock and M. F. Mason describe experiments on animals to determine the effect of extreme heat and cold on shock. Three methods of inducing shock were used. In the first approximately one-third of the blood volume was removed under an anaesthetic, during 30 minutes, and heat (6.6° F. elevation) and cold (2.2° F. depression) applied to two groups of animals. All those subjected to heat and cold and 9 out of 14 controls died. The duration of life was longest in the 'cold' group and shortest in the controls. In the second series, blood pressure was reduced uniformly to 74 millimetres of mercury. Seven animals were subjected to heat, 6.8° F. elevation, with 7 controls, and 11 subjected to cold, 10.6° F. depression, with 11 controls. They all died except 2 of the 11 controls. The average duration of life of the cold animals was 16 days, compared with 11, for the controls, and of the heated animals was 3 hours 50 minutes, compared with 8 hours, for the controls. In the third series 8 animals were exposed to trauma and heat, 2.8°–9.8° F., and 15 to trauma and cold, 11.8° F., depression. Those exposed to cold lived twice as long as those exposed to heat; one of them recovered. Attention is drawn to the striking fact that the heated animals died soon after the critical level of hypotension, whereas the cold animals' death followed a long period of hypotension. There was intestinal haemorrhage and the venous blood was bright in colour.

The phenomenon of vasoconstriction accompanying shock indicates a diversion of blood supply to the vital organs. It is concluded therefore that the application of heat will withdraw this vital supply. Heat, moreover, aggravates the development of oedema which is another drain on blood supply. Vasodilatation has been observed on the application of heat. Cold, moreover, reduces the metabolic rate and with it, the oxygen requirement of the tissues. The author does not condemn the practice of warming a shocked patient, but gives a warning against the application of excessive heat, especially to the extremities.

Pre-operative administration of cortin.—P. C. Corrado reports on the use in 33 cases of adrenal cortical hormone for the preparation of patients for major surgical operations. The dosage was 3 tablets daily for periods of 10 to 30 days before operation. This was supplementary to the usual preparation, given to all patients, of special diet, rest, and, in some instances, Lugol's solution. Patients given the adrenal cortical hormone withstood the strain of anaesthesia and operation much better than those who did not receive this treatment; the blood pressure, pulse rate, and plasma volume, as measured by red cell counts and percentage of haemoglobin, fluctuated much less than in the controls. The hormone probably acts by enabling the patient to maintain a better regulation over the fluid and electrolyte balances of the blood and tissues with little change from the normal in cell membrane permeability. This would be in keeping with the recognized action of the adrenal cortical hormone in experimental animals.

Secondary shock

Plasma and blood transfusions.—A. Kekwick, H. L. Marriott, W. d'A. Maycock, and L. E. H. Whitby in an investigation of 24 cases of secondary shock, found that a serious fall in blood pressure was the one reliable clinical criterion of the severity of the condition. The pulse rate was unreliable. As a rough rule, a rise of 10 to 20 millimetres of mercury can be anticipated from every 540 cubic centimetres of blood transfused, provided that bleeding has ceased and that there are not any other causes of loss of circulatory fluid. Plasma and blood are equally effective for the restoration of the blood volume.

Postural.—A. R. MacLean, W. McK. Craig, and E. V. Allen discuss the problem of venous return and its clinical importance. The upright posture, with a consequent pooling of blood in the lower extremities, makes venous return precarious. Failure brings about symptoms of shock and hypotension. This has been observed after sympathectomy for essential hypertension and is not due to arteriolar contraction, but to the pooling process. Recumbent posture gives momentary relief but diminishes the efficacy of compensating mechanisms, for example, the production of extra-cellular fluid which supports the tissues in the lower extremities. A semi-erect position is recommended for patients with poor venous return or about to undergo a major operation, to alleviate subsequent shock. The 'head up' posture has been used in nursing intracranial pressure cases and for some operations, but fluctuations in blood pressure often necessitate a return to the prone position. To obviate this a new method was tried of maintaining blood pressure during operations: after 48 hours in the 'head up' posture the patient was anaesthetized and while recumbent the lower extremities were elevated and firmly bandaged from the toes to the groins. During the operation nothing was administered for blood pressure changes in spite of considerable blood loss. The method has been used with success on several occasions.

Intravenous transfusions

Comparison of saline and serum.—D. K. Hill, J. McMichael, and E. P. Sharpey-Schafer found that physiological or hypertonic saline, given intravenously to normal people, was rapidly lost from the circulation, whereas serum, given intravenously, was retained for long periods. The rise in blood-volume following serum administration depended on the total

amount of protein added, and was independent of the dilution of serum employed. In patients with shock, intravenous saline produced only transitory benefit. Serum was very effective in overcoming circulatory collapse due to diminished blood-volume. The recovery of a shocked patient was invariably heralded by a rise in systolic and pulse pressures. The pulse rate is a deceptive index of the patient's condition, since it often remains high even when the blood pressure has risen to normal.

Hypertonic saline.—R. A. King compared experimentally various methods of fluid administration in the treatment of surgical shock. He confirmed the temporary beneficial effect of intravenous saline. Hypertonic saline given intravenously stimulates the circulation in shock. The rise in blood pressure is probably prolonged by osmotic absorption of tissue fluids. Fluids absorbed by the capillary circulation from the intestines or subcutaneous tissues may restore blood pressure permanently in shock. In severe shock no absorption occurs by the capillaries. The author adduces some evidence that hypotonic saline may be absorbed by the tissues in severe shock and produce a sustained rise of blood pressure when the circulation is stimulated by hypertonic saline and an osmotic gradient is maintained.

Transfusion and a vasoconstrictor

J. C. Meakins recommends that dehydration in shock should be prevented or removed by saline infusions *before* operation, that transfusions of whole blood and saline infusions are indicated, but have a limited value after shock has developed, although the first is particularly indicated in haemorrhage, and points out that potent extract of the adrenal cortex would seem to strike at the root of the matter by correcting the abnormal capillary and cellular permeability. He emphasizes the promising character of the concentrated blood serum, advocated by C. H. Best and D. Y. Solandt on experimental grounds in an earlier paper. The latter workers consider that in severe shock the initial treatment should be the administration of a vasoconstrictor, and that, unless the blood pressure is very low, pituitrin is preferable to ephedrine, before the administration of concentrated human serum prepared by the Thalhimer technique.

Pooled concentrated human serum

B. Rose, P. G. Weil, and J. S. L. Browne treated 13 cases—5 of shock—with pooled concentrated human serum. In another the patient received concentrated typed human serum. The authors observed reactions in 5 patients, or 35 per cent of the whole, and death occurred in 2 of these. In the other patients, in whom no reaction was noted, the serum appeared to be beneficial in 7. The authors consider that this type of serum is contra-indicated in the therapy of shock because of the frequency and type of reactions produced.

Choice of anaesthetics

E. M. Chivers and W. E. F. Evans state that patients in surgical shock should not be given anaesthetics unless immediate operation is essential; the correct anti-shock treatment should be given before such an operation. Intravenous barbiturates should be regarded with some suspicion. The most satisfactory anaesthetic is gas and oxygen by means of a closed circuit apparatus, and ether and divinyl ether should be employed to give more relaxation when required. Since oxygen lack greatly increases the degree of shock, the airway must be kept free from obstruction; the oxygen content of the required mixture must be kept high, and the resistance of the circuit kept low.

Paredrinol in experimentally produced shock

Effect on circulation.—In the Supplement 1940 (p. 529) an abstract was given of some of the investigations carried out in the Medical School of Harvard University on the pharmacology of paredrinol (α -N-dimethyl-*p*-hydroxyphenylethylamine) which produces a generalized arteriolar constriction with arterial hypertension and without changes in the cutaneous temperature, oxygen consumption or cardiac minute volume, and has been employed in the treatment of shock and collapse artificially induced in man and also, though to a much less degree, in advanced circulatory failure in acute infections. E. A. Stead, Jun. and R. V. Ebert report further observations, made on six normal voluntary subjects, on the action of paredrinol after the production of haemorrhage and circulatory collapse. The amount of intravenous paredrinol necessary to induce a definite rise in arterial blood pressure was determined for each subject when in the normal state. Next day 760 to 1,220 cubic centimetres of blood, or 15 to 20 per cent of the total blood volume, were removed by venesection. Three to 60 minutes later the same quantity of paredrinol used in the control test was injected intravenously. It is pointed out incidentally that there is not any danger in rapid removal of large quantities of blood from normal subjects by venesection, because, if circulatory collapse occurs, the sharp fall in arterial pressure will prevent the loss of any more blood from the venous system; normal persons always recover spontaneously from this form of collapse. In 5 of the 6 subjects circulatory collapse occurred either during or a few minutes after venesection; one became unconscious. The blood pressure fell precipitately and the pulse became very slow. In two subjects the collapse was not treated and spontaneous recovery followed. In 3 subjects paredrinol was injected at the height of the collapse, in 2 the arterial blood pressure was 62 systolic and 40 diastolic and 50 systolic and 30 diastolic millimetres of mercury, and in the third could not be obtained; in each case the systolic pressure rose to 100 millimetres of mercury within 3 minutes of the injection, but did not reach the level before venesection. The conclusion is drawn that the lack of clinical improvement in patients

with severe circulatory collapse from acute infections is due, not to a simple reduction of blood volume, but to a combination of factors.

A. Iglauer and M. D. Altschule report on the reactions of the pulmonary blood content to the oral administration of paredrine, a sympathomimetic amine, in 5 normal subjects from 23 to 35 years of age. The question arises whether or not the wide-spread vasoconstriction causes redistribution of the circulating blood, and it is pointed out that the use of paredrine (*p*-hydroxy- α -methylphenylethylamine hydrobromide) has been suggested in conditions in which it is desirable to raise the blood pressure without increasing the cardiac output directly. From observations, including gas analyses the authors conclude that doses of paredrine sufficient to cause marked changes in the blood pressure did not produce any significant change in ventilation, oxygen consumption, total pulmonary capacity or any of its subdivisions.

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SILICOSIS

See also B.E.M.P., Vol. XI, p. 133; and Surveys and Abstracts 1939, p. 537; 1940, p. 529.

Aetiology

Incidence and susceptibility

Miners of bituminous coal.—B. G. Clarke and C. E. Moffet, studying the chest X-rays and occupational histories of 774 workers in bituminous coal in order to determine to what extent silicosis was present, and employing as controls the physical examination and X-ray records of 774 steel-plant workers, conclude as follows: these miners are prone to develop pre-silicotic and silicotic lung changes after prolonged employment, 2 per cent of the miners showing pre-silicotic changes and 1 per cent silicotic nodulation in the chest X-rays. These changes occurred chiefly among undercutting machine operators and coal loaders. The shortest period of exposure necessary to produce nodulation was noted in a rock driller who had worked at his trade for 11 years.

Morbid Anatomy

R. J. Ritterhoff reports 2 fatal cases in men, aged 18 and 28 years, with so-called 'acute' silicosis, confirmed by necropsy, after exposure during work in the abrasive soap powder industry for 100 days and 12 months respectively. One of the 2 cases was complicated by a tuberculous empyema and acute caseous tuberculous broncho-pneumonia. The other patient was free from tuberculosis, and presented cor pulmonale, enlarged right ventricle and auricle, in addition to massive confluent pulmonary silicotic fibrosis with prominent emphysema. These 2 cases brought the number of similarly proved cases to 8, in 3 of which cor pulmonale was present; in 9 cases, not confirmed by necropsy, 3 had shown definite evidence of right-sided cardiac failure. Out of the 8 proved cases 3 were free from evidence of pulmonary or other forms of tuberculosis. The 2 reported patients had a history of exposure to the soap powder considerably shorter than the other cases, both confirmed and unconfirmed, and their survival after cessation of exposure, namely, 4 years, was considerably longer than in the unconfirmed cases. Analysis of the soap powder to which the 2 patients had been exposed showed free silica 60 per cent, Italian pumice 30 per cent, and 'kettle soap' 10 per cent.

Clinical Picture

Acute silicosis

Rapid onset in a sand-blaster.—W. D. McNally reports a case of silicosis in a sand-blaster becoming acute in under 4 years. The usual period for the development of acute silicosis is 9 years or more in mining, sand-blasting or quarries. The patient, aged 26, was employed as a sand-blaster for over 3 years and was inadequately protected against dust. Early symptoms, with shortness of breath and chest pains, were shown after 12 months. X-ray films demonstrated after 12 months blotched lungs, particularly at the lower and middle lobes, but clear

apices. After 24 months the upper lobes were slightly affected. Films taken after 34 and 37 months showed the apices completely affected indicating the onset of acute silicosis. The author concludes that the patient should not have worked in dust after 12 months and that the prognosis is poor, since the progress of the disease is likely to go on even after removal of the patient from the dusty atmosphere.

Tuberculo-silicosis

X-ray findings.—L. Benson reports observations on 207 employees in the granite industry who had silicosis complicated by pulmonary tuberculosis. The clinical forms of tuberculo-silicosis often resemble those in pulmonary tuberculosis, without silicosis. The commonest form of tuberculo-silicosis in granite workers is that in which there is a very slow progression of the infective process. Many of these cases appear in patients who have previously shown localized discrete areas by X-rays accompanying nodular shadows of simple silicosis and suggesting the occurrence of silicosis superimposed on inactive tuberculosis. Bilateral nodular shadows in X-ray films of granite workers are usually due to simple silicosis; it is, however, difficult by a single film to differentiate early uncomplicated silicosis from tuberculosis. The only absolute clinical proof of tuberculosis is the presence of tubercle bacilli in the sputum; but direct smears usually do not give positive results unless there are at least 100,000 bacilli per cubic centimetre, hence frequent concentrations and injection into animals are necessary. There appears to be a high correlation between the X-ray evidence of cavities in tuberculo-silicosis and bacilli in the sputum. In cases of silicosis preceded by short exposures to high concentrations of silica followed by early death, microscopic sections obtained from material removed at necropsy may show silicotic lesions not visible radiologically. A rare form of tuberculo-silicosis in granite workers is that in young men with an acute onset, severe dyspnoea, cough, and fever. There is little sputum and films taken before the onset of symptoms show the nodular lesions of simple silicosis; whereas radiograms taken after the onset of acute symptoms show rapid coalescence of the nodular shadows. It is suggested that this form of tuberculo-silicosis may be the result of a primary or lympho-haematogenous infection in a patient with silicosis and very little resistance to tuberculosis.

The treatment of tuberculo-silicosis is said to be the same as that of pulmonary tuberculosis. Patients with the early infection should undergo complete rest in bed to determine the stability of the lesion by daily temperature charts, weekly weighings, sputum and blood tests, and radiograms; for this three to six months may be necessary. The more advanced cases should if possible be treated by ambulatory methods.

Benson, L. (1940) *New Engl. J. Med.*, **223**, 398.

Clarke, B. G., and Moffet, C. E. (1941) *J. industr. Hyg.*, **23**, 176.

McNally, W. D. (1941) *J. industr. Hyg.*, **23**, 45.

Ritterhoff, R. J. (1941) *Amer. Rev. Tuberc.*, **43**, 117.

SIMMONDS'S SYNDROME

See also B.E.M.P., Vol. XI, p. 145; Surveys and Abstracts 1939, p. 538; 1940, p. 530; and p. 92 of this volume.

Clinical Picture

Spontaneous hypoglycaemia

E. Mogensen describes the case of a woman, aged 48, with symptoms of Simmonds's syndrome, but without pituitary tumour, in whom attacks of spontaneous hypoglycaemia occurred. Amenorrhoea had been present for 20 years; pubic and axillary hair was absent; the genital organs were atrophied. The patient had lost weight, was debilitated, and looked old; the skin was atrophic and dry. The basal metabolic rate was about -20 per cent, blood pressure 100/60 millimetres of mercury and the red cell count 3.1 millions. Her mental condition was usually normal at first, then she grew nervous and irritable and finally delirious. In such attacks the blood-sugar fell to 45.43, and even 38 milligrammes per 100 cubic centimetres. Further hypoglycaemic attacks were avoided by frequent meals and the patient was able to return home. Treatment with gonadotrophic hormones and with oestrin failed to produce any considerable improvement. The author regards the abnormality in blood-sugar as due to reduction of the hormone of the anterior pituitary which raises the blood-sugar, the diabetogenic hormone. He therefore tried an alkaline extract of anterior pituitary which he expected to have some diabetogenic effect, but this did not produce any satisfactory rise in the blood-sugar.

Mogensen, E. (1940) *Endocrinology*, **27**, 194.

SKIN DISEASES: AFFECTIONS DUE TO INSECTS AND ACARINES

See also B.E.M.P., Vol. XI, p. 149; and Surveys and Abstracts 1940, p. 531.

The Occasional Attacker

Acarines

Infection from cats.—J. H. T. Davies reports 5 cases of cat itch resulting from contact with cats infected with *Cheyletiella parasitivorax* or *Notoedrus cati*. The clinical appearances of both diseases in the human subject are much the same. The essential lesion is an urticarial papule, generally small, exceptionally like that of strophulus, which quickly disappears, leaving a tiny prurigo papule. The top may be scratched off, leaving a small crust but, apart

from this, there is a striking absence of secondary scratch lesions or infection. The eruption appears in crops having a relation to contact with the animal, and the distribution may be of the generalized or opportunist variety in either case. Both diseases rapidly disappear on removal of the offending cat.

Parasites Breeding on Human Host

Acarus scabiei

Benzyl benzoate therapy.—According to R. E. King, the benzyl benzoate treatment of scabies has many advantages over other methods; the patient is ambulant throughout treatment, and is subjected to a minimum of discomfort, no matter how severe the infection. The sarcopticidal action of the drug is immediate and reliable, and does not irritate the skin. Pyodermitis due to infected scabies can be thoroughly treated and rapidly cured, and the whole treatment is completed in 30 minutes at the cost of a few pence. The lotion consists of equal parts of benzyl benzoate, industrial spirit, and soft soap (B.P., 1932). The amount of this lotion used in the complete treatment of one case is an ounce and a half. The body is anointed with soft soap, those parts—groins, axillae, inner aspects of thighs, wrists, abdomen, interdigital spaces—commonly attacked by the acarus receiving special attention. The patient soaks for 10 minutes in a bath at 100° F., and thoroughly rubs the affected areas during this time. While the body is still wet, the lotion is vigorously applied for 5 minutes with a pig-bristle shaving-brush. The lotion and the lather produced is allowed to dry on the skin, and the lotion is again applied for 5 minutes, and the body dried with a towel. The patient then resumes the clothes worn before treatment. Twenty-four hours later a bath is taken and clean clothes are put on. In 100 patients, 80 per cent of whom were infected for more than 2 weeks, treatment by one application of benzyl benzoate lotion proved completely successful.

Derris root.—L. Saunders recommends the use of derris root in the treatment of scabies. The method is free from smell and from grease, inexpensive, obviates any need for disinfection of the clothes and baths, requires only 2 days, and is most effective. A solution consisting of 4 ounces of derris root in 1 gallon of cold water is made; to each $\frac{1}{2}$ pint of lotion used, 1 teaspoonful of soap flakes is added. The patient, without preliminary bathing, rubs the lotion with cotton-wool all over the body from neck to toes and allows it to dry. One application is made in the morning, afternoon, and evening for 2 consecutive days. The patient wears his own clothes.

Treatment by rotenone.—C. C. Thomas and E. E. Miller report on the use, as a local application, in scabies of a 1 or 2 per cent solution of the insecticide rotenone, which is one of the active principles of derris or tuba root (*Derris elliptica*). It was employed locally in 24 unselected cases of scabies. Cure followed in all the cases, and in the majority within 3 or 4 days. L. Saunders adopted this treatment in a modified form; instead of the insecticide rotenone he made a suspension of the powder obtained from derris root. This was rubbed over the whole body by the patient and allowed to dry on the surface, a thin coating of the powder being left on the skin. The disadvantage of this method is that some patients complain of a burning sensation in the scrotum and penis after 4 or 5 applications; this is probably met by further dilution. There are many advantages, namely absence of smell, grease, and messiness, no staining of underclothes and bed-clothes; cheapness, each course costing about a penny; obviates baths and disinfection of clothes; and rarity of relapses.

Acarus scabiei and *pediculosis*

Treatment.—At a discussion before the Dermatology section of the Royal Society of Medicine on the louse and scabies, it was agreed that the problem was a civilian rather than a service one. But there was not any real evidence of an increase in their incidence in air-raid shelters. P. A. Buxton opened the discussion with an account of experiments on louse incidence in samples of hair from Africa and Asia. Age and the weight of hair seemed to be the only significant factors. Lice had been kept under observation in closed cells attached to the human skin. He quoted the work of two entomologists—McLeod and Craufurd-Benson, who started a louse clinic in East London, and used a new insecticide powder, A.L. 63, which would make a garment proof against lice for a week. H. J. Craufurd-Benson noted that an insecticide which would kill lice in the laboratory will not necessarily kill them when used on a verminous person. An insecticide that worked well in the laboratory might be quite hopeless in the field. Breeding conditions were considered to be the most important factors by A. M. H. Gray, who thought that elementary cleanliness was an adequate precaution in shelters. The fall in the incidence of scabies after the last war followed by a steep rise in 1938 to the 1919 level was noted. This was partly attributed by F. A. E. Silcock to migration from industrial areas during the depression and recently during evacuation. F. F. Hellier considered the increase to be cyclic and on a world scale. F. S. Airey suggested that post-war practitioners were not so well experienced in dealing with scabies. H. MacCormac compared the head louse, pubic louse, and body louse. The first was easily disseminated but not dangerous, the second was less mobile, frequently of venereal origin, and could be spread by unclean lavatories and bedding, but it could not survive long without a host. The body louse could live freely for a time, was mobile, and threatened to make trench fever and pyoderma a real danger in shelters. Scabies could not be spread by mere casual proximity, and its diagnosis might be very easy, but that of secondary impetigo was difficult. Scabies could then be distinguished from pediculosis because the impetigo of scabies tended to be grouped over the elbows, knees, and lower buttocks, whereas pediculosis affected the shoulders, lumbar

regions, and thighs. A latent form of scabies had been observed by G. B. Mitchell-Heggs and H. W. Gordon. Various treatments were recommended. Although there was support for disinfection of clothing and bedding, Gordon and the President (W. J. O'Donovan) did not consider it necessary in all cases. Three-day treatment with sulphur ointment was recommended by MacCormac who criticized the benzyl benzoate 1-day treatment because the egg took 3 days to hatch. Scrubbing with soft soap and benzyl benzoate or even soft soap alone for 3 days was suggested by Silcock. Gordon had observed cases of acute dermatitis resulting from sulphur treatment. A. M. Stuart suggested 40 per cent sodium thiosulphate and 4 per cent hydrochloric acid preceded by soft soap, and Marcussen's ointment was suggested as a substitute for sulphur ointment by the President. The need for an insecticide which remains effective long enough to kill adult insects and larvae was emphasized by Craufurd-Benson and re-emphasized by Buxton in winding up the discussion.

Airey, F. S. (1941) *Proc. R. Soc. Med.*, **34**, 202.

Buxton, P. A. (1941) *Proc. R. Soc. Med.*, **34**, 193.

Craufurd-Benson, H. J. (1941) *Proc. R. Soc. Med.*, **34**, 200.

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SKIN DISEASES: OCCUPATIONAL DISEASES

See also B.E.M.P., Vol. XI, p. 161; and Cumulative Supplement, Key Nos. 1405-1408.

Cancer

Causes

Mule-spinner's cancer.—E. M. Brockbank gives the results of his experience, as a medical referee for industrial diseases, of more than 150 cases of cutaneous epithelioma (squamous-celled carcinoma), especially of the scrotum, among mule-spinners. The reports of the Inspector of Factories show that during the 17 years ending 1939 the average annual incidence was 64 cases with 21 deaths; in 1939 there were 52 cases with 20 deaths. As a medical referee Brockbank saw 16 cases in 1940, and points out how disappointing is the continual incidence of this preventable disease. Of the scrotal cases 80 per cent occur on the left side; this is due to the conditions of work among mule-spinners, namely more exposure of the left side to contact with mineral oil, and the tendency of excessive perspiration from the lower abdomen to run down the left rather than the right side of the scrotum; the importance of the last factor is that sweat washes off secretion from the sebaceous glands and so allows close access of mineral oil to the skin. Heat and excessive sweating alone do not cause the disease, as coal-miners are remarkably free from it. Dry skin, especially in older subjects, and ichthyosis are disposing factors. Preventive measures include periodic medical examinations, often requiring biopsy and histological investigation; selection of the safer oils or blends recommended by the Manchester Committee's scientific staff; protection of the skin from contact with mineral oil. This may be done by an additional trouser garment and (2) a protective ointment, such as a mixture of lanolin and olive oil to the unwashed skin before exposure to the mineral oil, in men 50 or more years old, and those with specially dry skin, of whom there are, however, comparatively few at work. Advisory handbills about mule-spinner's cancer are also recommended.

Brockbank, E. M. (1941) *Brit. med. J.*, **1**, 622.

SKIN DISEASES: LOCALLY INOCULATED INFECTIONS

See also B.E.M.P., Vol. XI, p. 183; Cumulative Supplement, Key Nos. 1409-1410; and Surveys and Abstracts 1940, p. 532.

Phagedaenic Ulcer

Progressive bacterial synergistic gangrene

M. E. Lichtenstein reports a case of progressive bacterial synergistic gangrene which is a chronic, rapidly spreading necrosis of the skin. The gross appearance of the lesion is that of a necrosis of the dermis after destruction of the superficial layer of fat. The patient, a man aged 50, had been operated on for acute appendicitis, and, after 17 days, showed a 'pimple' to the left of, and above the umbilicus. During the following 2 weeks this took on the appearance of a carbuncle, enlarged rapidly, and sloughed in its central portion, leaving an ulcer with a necrotic edge. The lesion spread rapidly but did not invade the area of the scar or the umbilicus. Histologically the margin of the ulcer contained many polymorphonuclear leucocytes, chromatin debris, and islands of swollen and oedematous epidermis. Streptococci,

staphylococci, and diplococci were obtained on culture. The whole lesion was excised, and the wound treated with zinc peroxide cream. A clean granulating surface was produced, and Thiersch grafts were applied.

Lichtenstein, M. E. (1941) *Arch. Surg., Chicago*, **42**, 719.

SKIN DISEASES: TUMOURS

See also B.E.M.P., Vol. XI, p. 200; Cumulative Supplement, Key Nos. 1412-1415; and Surveys and Abstracts 1939, p. 539; 1940, p. 533.

Innocent Tumours

Derived from superficial layers

X-rays and radium therapy for plantar warts.—E. A. Oliver claims that X-rays and radium are the methods of choice in the treatment of plantar warts. Since warts are infections caused by a virus, other methods, such as surgical excision, may open up new channels of infection. Since they do not cause pain, these methods are particularly suitable for children. One unfiltered X-ray exposure was given to 123 children; the dosage varied from 2 to 3 skin units (700 to 1,050 roentgens). In these cases there were only 2 failures, or 98.3 per cent successful results. One radium exposure, varying in time from 1½ to 2 hours, was given to 64 children, and cure resulted in 100 per cent of the cases. The results in the treatment of adults were correspondingly successful.

Derived from fibrous tissue

Dermatofibroma.—J. F. Stecker and W. L. Robinson, who write with experience of 62 cases, define this tumour of many names—fibroma simplex, nodule cutanei, dermatofibroma lenticulare, nodular subepidermal fibrosis—as a small, hard, fairly well circumscribed lesion originating as a benign growth in the corium of the skin and having certain features characteristic of a simple fibroma, yet being unencapsulated, infiltrative, and slowly growing. The nodule is usually solitary, though 10 to 20 have been recorded; 41 of the 62 cases, or 68 per cent, occurred on the extremities, 20 per cent on the chest and trunk, the head, neck, and face being affected the least. The nodule varies from 2 to 3 millimetres to 1 to 1.5 centimetres in maximal diameter. Usually it is firm, spherical, and pink, brown, or dark red. The patients' ages ranged from 21 to 76 years. Pain is rare and with adequate excision there is not any recurrence. Microscopically the nodule rests in the subepidermal area of the skin, and is made up of large irregular spindle-shaped cells running in many directions; they are large but not comparable to those of malignant growths. The nuclei are large; mitosis is rare. The margin of the nodules is ill defined and the peripheral cells infiltrate the surrounding collagen and spread round the coil glands. Clinically it may be confused with melanoma, keloid, angioma, neurofibroma, and more seriously with carcinoma, sarcoma, or rodent ulcer. In 28 cases in which a diagnosis was made before removal, 10 tumours were regarded as malignant.

Derived from hair follicles

Multiple benign cystic epithelioma.—H. J. Goldman found that in 4 generations of a family consisting of 19 members, there were 10 cases of multiple benign cystic epithelioma. Transmissions occurred in both males and females and the incidence in both sexes was the same. Microscopical examination of material from 7 of the patients showed that 5 exhibited the picture of tricho-epithelioma. The most conspicuous histological abnormality was dilatation of the hair follicles with its central keratinous nest. The appearance of keratinous nests within basal-celled tumours should always suggest tricho-epithelioma, whether seen in connexion with multiple benign cystic epithelioma or not.

Derived from nerve tissue (glomus tumours)

Three papers recently appeared in the *Canadian Medical Association Journal* on these benign growths of normal glomus bodies in the skin which appear a few months after birth, become fully developed in early adult life, and atrophy with age (Blanchard). They consist of specialized arteriovenous anastomoses through which blood is shunted directly from the arterioles to the venules without passing through the capillaries. They also contain non-medullated nerve fibres, and J. H. Couch, who reports a case, draws attention to the occurrence of Horner's syndrome in connexion with glomus tumours, which are most often present in the hands and feet and inhibit the secretion of sweat, and so influence the loss of body heat. The histological features are illustrated by Blanchard both in the normal glomus and in the glomus tumours with proliferation and enlargement of the glomus or epithelioid cells. B. Plewes, who states that less than a hundred multiple glomus tumours have been recorded, reports a case in which there were 4 glomus tumours in one finger-tip of a boy 16 years of age, and quotes 5 other cases of multiple glomus tumours. Nabarro recorded a case in a woman, aged 38 years, who had often been examined during 12 years before the condition which caused wide-spread tenderness and pain was detected and operated upon. It is pointed out that these glomus tumours were described in 1812 by W. Wood as 'painful subcutaneous tubercles'.

R. E. Swenson reports a glomus tumour in a woman aged 28. It was unusual in its location, being situated below the fat pad of the left middle finger, almost on the anterior surface of the bone. Another unusual feature was that, except for extreme tenderness, there were not any physical signs of its presence, and it was discovered only on operation.

On synovial membrane of knee.—H. O. E. Hoffmann and R. K. Ghormley describe the case

of a man, aged 52 years, who in 1916 received a severe blow on the inner side of the right knee; two weeks later acute tenderness and pain began in the area of the injury; for 24 years the patient suffered daily from severe pain in a rather sharply localized area, excruciating pain being produced by the slightest pressure, even splashing of water in a bath. In 1918 a cartilage had been removed from the knee joint, in 1919 'neurolysis' was performed, and in 1928 some superficial tissue was excised from the tender, painful area. No relief followed these operations, and the patient was greatly depressed and threatened 'to end it all' unless he could get sufficiently relieved to return to work. Exploration of the knee joint led to removal of a glomus tumour the size of a Lima bean from the synovial membrane, and to complete freedom from pain. Ghormley adds that the glomus tumour or glomangioma is 'an overgrowth of a specific arteriovenous anastomosis and the neurones terminating in it', and has been regarded as part of the heat-regulating system of the body and as playing some part in the regulation of blood pressure; that they usually occur in the subcutaneous tissue and in the extremities, about 30 to 40 per cent occurring under the nails.

Malignant Tumours

Derived from superficial layers of epithelium

Precanceroses.—O. S. Ormsby discusses the various skin lesions which though originally benign may become malignant. Among the hyperkeratoses, senile keratosis is the most likely to become malignant. Both syphilitic and non-syphilitic leucoplakia are also important conditions. Among the pigmented moles, the most dangerous form is the flat and slaty or blue-black one; as a rule chronic irritation or trauma is an associated factor. Other conditions are keratosis follicularis, Paget's disease of skin or nipple, erythroplasia of Queyrat, xeroderma pigmentosum, arsenical keratoses, paraffin dermatitis, and X-ray keratoses.

Precancerous leucoplakia and keratoses.—F. B. Bogart states that precancerous leucoplakia and keratoses are, as a rule, best treated by electrocoagulation. Individual areas of keratosis which appear to be undergoing malignant change should, like cancer, be treated with large doses of irradiation. Comparatively small basal- or squamous-celled carcinomas are treated with large doses of X-rays generated at low or medium voltage with little or no filtration. Carcinomas involving cartilage, carcinoma of the lip, and the 'radio-resistant type' of squamous-celled carcinoma are treated with X-rays, generated at high voltage, 200 kilovolts, using heavy filtration.

Carcinoma

X-ray treatment.—P. E. Wigby and M. Cohen, from analysis of 83 carcinomas of the skin in 70 patients treated by X-rays, state that basal-celled carcinomas should receive at least 4,000 roentgens and preferably 5,000 roentgens of low voltage (90 to 130 kilovolts), using a combination of no filtration and a 1 millimetre aluminium filter at the first treatment, or first series of treatments. Intradermal, adenocystic, infiltrating basal-celled and squamous-celled lesions should receive between 5,500 and 6,500 roentgens, using medium and high voltage X-rays and from a 0.5 millimetre aluminium filter to a 2 millimetres copper filter, and giving about 200 roentgens daily. Small lesions may be treated by large daily doses (1,000 roentgens the first day and 600 roentgens daily thereafter).

H. B. Hunt states that large protruding carcinomas in the basal-celled areas often show an alveolar arrangement of basal-celled lesions combined with keratinizing features. Bulky squamous-celled carcinomas tend to be moderately to highly anaplastic, and show an abundant delicate vascular network which is associated with moderately high radio-sensitivity. The prognosis is reassuringly good, since metastases to regional lymphatic glands are remarkably infrequent, in view of the size and activity of the primary lesion. Deformity following eradication of the neoplasm by irradiation is surprisingly little, being due to superficial invasion only of healthy tissues by the growth. The tumours can be successfully treated by X-rays, radium, surgery, or a combination of these agents.

Significance of skin colour.—J. Taussig and G. D. Williams estimated by means of a colorimeter the skin colour of the forehead, arm, and back in 100 unselected cases of skin cancer and 100 non-cancerous patients of similar age. It was found that the exposed skin of the foreheads and arms of patients with skin cancer was, on the average, definitely redder and darker than that of the non-cancerous. The unexposed skin of the backs did not show any such difference. The cancerous patients were more often exposed to the action of the external environment than were those of the controls. This suggests a probable causal connexion between exposure of skin and the production of skin cancer. Subjects whose skins on unusual exposure tend to darken and redden, if they show skin cancer, more often exhibit the basal-celled or the mixed forms, whereas those who do not react to unusual exposure more often show the squamous-celled type.

Innocent Infective Conditions

Sarcoids

Multiple benign sarcoid of Boeck.—G. E. Lewis records an unusual case, in a woman aged 53, of sarcoidosis with signs and symptoms suggesting involvement of the central nervous system and the production of Adie's syndrome (myotonic or pseudo Argyll Robertson pupil). Some speculations are discussed as to the stages of infection in general. The patient gave a negative blood and cerebrospinal fluid Wassermann reaction, a negative Mantoux reaction, and had attacks of episcleritis and uveo-parotitis; the clinical features of Adie's syndrome

were recognized. It is suggested that the conditions in this and other cases of sarcoidosis represent a non-specific second stage of infection.

According to J. H. Palmer, who reviews the clinical groups of Boeck's benign sarcoid, a number of rare syndromes, described by the particular specialists in whose field they appeared to lie, have been now integrated into one disease. These inclusions, such as uveo-parotitis and Schaumann's disease, are united by the same histological structure, viz. granulomatous. Practically every organ and tissue of the body may be involved—the nervous system, especially by facial paralysis in uveo-parotitis; the lungs, in which a well-marked discrepancy has been described between the extensive changes shown radiologically (enlarged hilar glands, 'marbling' of the lung parenchyma, and small nodules throughout both lungs) and the patient's good condition and the slight or absent auscultatory signs; the heart; abdominal organs; splenomegaly and Crohn's regional ileitis; kidneys; bones, muscles, and tendon sheaths, as well as the well-known more superficial lesions. There is a high proportion of negative tuberculin reactions, and it has been thought that a virus infection is responsible.

W. F. Hollister and G. T. Harrell report a case of generalized Boeck's sarcoid. The patient died suddenly, and at necropsy the lesions of sarcoid were found in nearly all the organs, including a joint capsule and the epiglottis. Several caseous lesions were found in the liver and spleen. Tubercle bacilli were recovered in guinea-pigs inoculated with material from a lymphatic gland from the hilum of the liver. The authors conclude that the patient may have had two diseases: localized tuberculosis from which organisms were recovered, and sarcoid, the aetiological agent of which is unknown. There was also a streptococcal bacteraemia which was not considered to be significant.

Systemic Conditions

Necrobiosis lipoidica diabetorum

Alice G. Hildebrand, H. Montgomery, and E. H. Ryneerson record 8 cases of necrobiosis lipoidica diabetorum seen since 1936 at the Mayo Clinic, and analyse the 78 reported since 1929 when the disease was first described by Oppenheim. It is a localized cutaneous lipoidosis accompanied in more than 87 per cent of the cases by diabetes mellitus, usually following the onset of that disease by months or even years, but sometimes, in about 20 per cent of the cases, the reverse relation in time is present. It is characterized by reddish papular or yellowish plaque-like lesions with central telangiectases, usually on the lower parts of the legs. Microscopically there are changes in the deep layers of the cutis, consisting of necrobiotic foci with granular degeneration of the collagen fibres, loss of elastic fibres, and the presence of extra-cellular lipoids. Absence of xanthoma of foam cells containing cholesterol and cholesterol esters differentiates these lesions from those of the xanthomatoses, except lipid proteinosis which presents a different clinical picture. The blood lipids have been within the normal limits in the 8 cases at the Mayo Clinic and in the majority of the cases reported elsewhere. More than 80 per cent of the 86 cases have been in women, and the usual age at onset between 10 and 40 years. Injury plays a definite part in from 12 to 16 per cent. Two views as to the pathogenesis of the condition have been suggested, (1) a primary vascular lesion, possibly due to a circulating toxin with secondary thrombosis, necrosis, and fat imbibition, and (2) a local lipid disorder in the skin based on a general disturbance in fat metabolism. Neither of these is regarded as satisfactory. The lesions run an indolent chronic course and are little influenced by local or by general anti-diabetic treatment.

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SPINAL CORD DISEASES

See also B.E.M.P., Vol. XI, p. 302; and Surveys and Abstracts 1939, pp. 120 and 543; 1940, p. 536.

Systemic Diseases*Subacute combined degeneration of the spinal cord*

Clinical and pathological features.—R. E. Hemphill and E. Stengel report in detail the clinical and pathological features of a woman, aged 47, who for 2 years had gradually shown a pseudo-tabetic syndrome with finally acute symptoms of an extensive affection of both cerebral hemispheres. Two months before death mental symptoms appeared, 10 days before death complete left hemiplegia with left-sided disturbance of sensation, dysarthria and dysphagia followed, and a week later there was right hemiplegia with sensory disorder. The blood picture was normal. The cerebrospinal fluid 17 days before death showed an increased number of cells and red blood-corpuscles. Gastric secretion was not examined. The condition was ascribed to an unknown dietetic deficiency. The necropsy showed subacute degeneration of the spinal cord, moderate lymphocytic infiltration in the spinal ganglia, and the proliferation of the cellular elements between the ganglion cells; a recent haemorrhagic exudate in the subarachnoid spaces of the frontal and parietal lobes, the exudate containing many polymorphonuclear and mononuclear cells; recent thromboses in the larger vessels in the affected areas of the subarachnoid space; a purpuric condition of the cerebral grey and white matter. The brain also showed demyelination, not of recent origin, in the white matter, obviously independent of the other changes; and in the peripheral nerves moderate degeneration of the myelin sheaths and the axis cylinders.

Spina Bifida*Meningocele*

Associated with craniolacunia.—E. C. Vogt and G. M. Wyatt found that in X-ray films of 120 patients with meningocele, craniolacunia was present in 43 per cent. Of 5,000 patients without meningocele, X-ray of the skull showed only 2 cases of craniolacunia. The condition was most common in association with thoracic meningocele and it was more often associated with myelo-meningocele than with simple meningocele. The presence of craniolacunia is an unfavourable prognostic sign in patients with meningocele.

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SPINE DISEASES AND DEFORMITIES

See also B.E.M.P., Vol. XI, p. 361; and Surveys and Abstracts 1939, p. 544; 1940, p. 536; and p. 14 of this volume.

Tuberculosis (Pott's Disease)*Treatment*

Spine-fusion operation.—W. E. Swift, in a review of the end results of the spine-fusion operation for spinal tuberculosis on 817 patients, reports that 71 per cent were followed up for at least 5 years and some even for from 10 to 24 years, and justified the following conclusions. The advantages of a successful spine-fusion are rest to the diseased area, early subsidence of the activity of the lesion, maintenance of the kyphosis at the minimal amount of deformity, growth of the vertebral bodies in the fused area in children, possibility that the patient may become ambulatory at an early date, and the attainment of a permanently normal X-ray appearance of the diseased vertebrae. Excellent results were obtained in 72 per cent of the children and in 53 per cent of the older patients.

Spinal Manifestation of Specific Bone Diseases*Protruded intervertebral disk*

Associated with osteitis deformans.—A. R. MacKay reports and comments on 2 cases of a protruded intervertebral disk associated with osteitis deformans (Paget's disease of bone)—the first examples of this combination recognized at the Mayo Clinic. Two men, aged 52 and 55 years, complained of low backache and were found to show osteitis deformans of the pelvic bones. There was also evidence pointing to narrowing of the cavity of the spinal canal by a protruded intervertebral disk, and recovery followed this correction. In both cases the symptoms might have been attributed to osteitis deformans, and the pain due to the protruded disk, operated upon by J. G. Love, would have persisted without any relief. It is, however, frankly admitted that the ultimate prognosis is doubtful on account of the presence of osteitis deformans.

Scoliosis*Treatment*

Conservative methods.—A. Steindler and C. W. Ruhlin treated by conservative methods 80 per cent of their patients with scoliosis, and only 20 per cent surgically. The conservative method employed was compensation-derotation. Of 100 patients so treated, 64 had mobile spines and 36 had rigid spines. As a result of treatment the compensation persisted in 80 cases, and failed in 20. The authors consider that the method is adequate to obtain compensation in suitable cases, and that it leads to definite maintenance of posture. The rotary deformity of the thoracic spine cannot at present be corrected. A later series of 21 cases with a follow-up of 2 years gave the following results: 4, or 19 per cent, were compensated on admission, and were treated only by support and muscle development, and all of them maintained correction; 17, or 81 per cent, were not compensated on admission, and were treated by manipulative correction, derotation, muscle development, and support. Of these,

only 1 patient with a congenital scoliosis and a hemi-sacralization of the 5th lumbar vertebra failed to respond.

Inflammatory Diseases

Epidural abscess

Diagnosis.—A. A. Bailey and J. G. Love report 2 cases suspected to be epidural abscess of the spine and confirmed by laminectomy which was extremely successful. In a review of the subject attention is directed to Dandy's work, including his addition to anatomical knowledge of the epidural space which lies dorsal to the spinal nerve roots and does not exist ventrally as the dura mater is firmly adherent to the vertebrae. Epidural abscess may be acute or chronic. Chronic epidural abscess is one of the rare causes of an insidiously developing transverse lesion of the spinal cord, especially tumours. The infective agents most often found have been *Staphylococcus aureus* and *albus*, *Diplococcus pneumoniae*, *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*), *Bacillus typhosus*, various streptococci, and actinomyces. In Bailey's 2 cases no organisms were found. Most of the lesions are metastatic in origin. The age incidence has been from 1 week to 67 years. Although the progression of the symptoms in the 2 cases did not differ from those of a tumour, the following points were in favour of epidural abscess: a history of inflammatory lesions elsewhere in the body; the patients seemed more ill than is usually the case with tumour of the spinal cord; the blood sedimentation was raised in one patient, and leucocytosis was present in the other; the cerebrospinal fluid in one case gave evidence of inflammation.

Acute osteomyelitis

Treatment.—E. C. B. Butler, I. N. Blusger, and K. M. A. Perry report a case of staphylococcal osteomyelitis of the spine in a man, aged 53. He complained of a band-like pain around the chest, and there was an angular deformity at the level of the 5th thoracic vertebra. Radiography showed complete collapse of the 5th and partial collapse of the 6th thoracic vertebrae. The patient was placed in a plaster bed, and given sulphathiazole, which appeared to cause some improvement of the general condition.

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SPLEEN DISEASES

See also B.E.M.P., Vol. XI, p. 401; Cumulative Supplement, Key Nos. 1446-1452; and Surveys and Abstracts 1939, p. 546; 1940, p. 541.

Anatomy and Physiology of the Spleen in Relation to its Diseases

Vascular changes associated with splenic disease

Splenomegaly.—A. O. Whipple reports observations on the circulation of the portal bed and of the spleen in relation to splenomegaly, made by members of the Spleen Clinic at the Columbia Presbyterian Medical Centre, New York. The details of the circulation in the spleen have been much discussed, and it has been variously stated that (1) there is an open circulation and no continuity between the terminal arterioles and the venous sinuses, the splenic pulp spaces providing the only link between the arterial and venous radicals; (2) that the arterioles empty directly into the venous sinuses, the vascular bed being a closed system, and (3) the more modern view of a combined type of circulation in the mammalian spleen, namely, an open component in the vascular bed which permits the flooding of the splenic pulp spaces with whole blood but with additional pathways available, by means of which the extra-vascular detour of the pulp spaces may be short-circuited by direct communication between the arterioles and the venous sinuses. Whipple's observations agree with the view, namely, that the splenic pulp spaces provide the only link between the arterial and venous systems in the mammalian spleen. The individual pulp spaces are the most variable structures in the spleen; for the most part they are tortuous, utterly irregular, and inconstant channels, much dilated, or when collapsed without a visible lumen. In these reticulum and reticulo-endothelial lined spaces the red cells come in contact with phagocytic leucocytes and histiocytes. Splenomegaly is not always a primary splenic disease, and discussion is confined to the splenomegalies in which the intermediary circulation of the spleen, namely, the terminal arterioles, the reticulum of the splenic pulp, and the venous sinuses play a dominant part in the pathogenesis of the abnormal spleen. In chronic hereditary spherocytic (haemolytic) jaundice the pulp spaces are enormously engorged with red cells and spherocytes which undergo haemolysis there. In the consideration of splenomegaly due to portal hypertension Banti's syndrome is discussed and it is pointed out that this term has been employed for conditions Banti did not describe. He regarded as pathognomonic a conspicuous thickening of the fibrillar reticulum around the central arteries of the Malpighian corpuscles (fibroadenia). Banti's syndrome is regarded as the result of mechanical obstruction to the flow of blood within the portal bed, intra-hepatic or extra-hepatic. The intra-hepatic lesion responsible for congestive splenomegaly is usually hepatic cirrhosis; in about 140 cases at the Clinic

Aneurysm of the splenic artery.—J. V. Seids and H. Hauser report 2 cases of aneurysm of the splenic artery, one of which was successfully treated by proximal ligation of the splenic artery. In the other case the aneurysm was quite latent and was discovered by routine X-ray examination of the spine. In a survey of 58,000 necropsies the percentage of aneurysm of the splenic artery was 0.05 and the percentage of aneurysms in general was 1.26. Ligation proximal, or both proximal and distal, to the aneurysm is the most conservative and usually effective method of treatment.

Enlargement

Hepato-Lienal Fibrosis

W. P. Thompson considers that Banti's syndrome is the result of a number of primary lesions which produce splenic vein hypertension, and is a secondary mechanical congestive splenomegaly; he cannot see any reason for the assumption that it is due to an unknown toxic agent. It is not justifiable to retain the concept of three stages in the disease. The author's experience is that hepatic cirrhosis is only one of several obstructive mechanisms; if it is not present as the obstructive mechanism at the time of splenectomy, it will not occur subsequently. He suggests that the terms Banti's disease and splenic anaemia be replaced by the term congestive splenomegaly.

A. Of Known Origin	{ Infective. Syphilis, leishmaniasis, schistosomiasis, malaria, tuberculosis Toxic. Alcohol, lead, phosphorus
B. Of Undetermined Origin	
(primary fibro-congestive splenomegaly with cirrhosis)	{ With prevailing congestion With prevailing fibrosis (Banti's disease)

Splenectomy.—E. H. Barg and J. W. Dulin consider that splenectomy is the best treatment for Banti's syndrome, and should be performed in the early stages, but it may be contra-indicated in elderly patients because of the high operative mortality. In 3 of the authors' patients over 60 years of age, however, the condition was greatly improved by operation. Splenectomy relieved ascites, but did not insure relief from gastro-oesophageal haemorrhages. Of 22 cases in which splenectomy was performed, there was an operative mortality of 27 per cent.

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Ravenna, P. (1940) *Arch. intern. Med.*, **66**, 879.
Seids, J. V., and Hauser, H. (1941) *Radiology*, **36**, 171.
Stephenson, R. W. (1940) *Lancet*, **2**, 648.
Thompson, W. P. (1940) *Ann. intern. Med.*, **14**, 255.
Whipple, A. O. (1941) *Trans. Studies Coll. Phys. Phila.*, 4 ser., **8**, 203.

See also B.E.M.P., Vol. XI, p: 419; Surveys and Abstracts 1940, p. 542; and p. 26 of this volume.

P. Manson-Bahr states that, in tropical sprue, there appear to be at least two factors: (a) determines the onset of glossitis and diarrhoea, and (b) causes the characteristic megalob-

cytic anaemia. From the analogy of other recognized megalocytic anaemias it is permissible to postulate that the specific anti-anaemic factor is absent, as in pernicious anaemia, by the proved observation that the anaemia of tropical sprue responds to the administration of the extrinsic factor (liver) as effectively as it does in Addisonian pernicious anaemia, but in most cases of sprue the effects are lasting in restoring complete haemopoiesis.

Treatment

Nicotinic acid

P. Manson-Bahr suggests the use of nicotinic acid in sprue on the following grounds: (1) the comparison which may be drawn between the principal manifestations of sprue and pellagra, especially as regards glossitis and stomatitis; (2) the almost instantaneous reaction of the sprue glossitis, as in pellagra, to nicotinic acid therapy; (3) the response of severe sprue to nicotinic acid, as shown by its effect on the glossitis and the return of the intestinal functions to normal, which raises the point whether the changes in the tongue are not essentially of the same nature as those in the bowel. The author advances the hypothesis that the sprue syndrome is mainly due to non-absorption, or destruction, of vitamin B₃ in the small intestine, and assumes that the disease recognized as tropical sprue represents the fully developed picture of small-intestine deficiency, and is presumably due to previous damage to the intestinal mucosa. He postulates that although the sprue syndrome is commonly met with in its most typical form in tropical residents, yet minor manifestations of the same process may occur elsewhere, and constitute the condition known as non-tropical sprue. He believes that cases of this nature are distinct from coeliac disease and idiopathic steatorrhoea, in that they react like tropical sprue to nicotinic acid therapy. The author treated 24 severe and typical cases of sprue with nicotinic acid, and 7 with nicotinic acid and riboflavin. The most striking effect of the nicotinic acid was on the glossitis, and the rapid return of the sense of taste to normal; the fiery redness of the tongue tended to fade in 24 hours, and the appearance to become normal in 3 or 4 days. In the glossitis of advanced sprue the addition of riboflavin appeared necessary to heal the angular excoriations. The dosage employed varied from 150 to 300 milligrams daily by mouth; the dosage of riboflavin was 3 milligrams daily. With regard to intestinal symptoms, diarrhoea ceased in 4 days, without the use of such therapy as colloidal kaolin, etc. Flatulence and meteorism were strikingly absent. Manson-Bahr advises that the treatment should be continued for about 3 months or longer, with a dosage of 150 milligrams of nicotinic acid daily for 14 days in each month, for 6 months. Toxic effects were remarkably few, and consisted of flushing of the face and slight roseolar rash. There was rapid improvement in the skin condition, and an increase in body weight. In 2 cases of non-tropical sprue similar satisfactory results were obtained with nicotinic acid therapy.

Manson-Bahr, P. (1940) *Lancet*, **2**, 317.

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STERILITY

See also B.E.M.P., Vol. XI, p. 447; Cumulative Supplement, Key Nos. 1455–1457; Surveys and Abstracts 1939, pp. 30, 157, and 548; 1940, p. 543; and p. 21 of this volume.

Sterility in the Female

Causes

Effect of pus on survival of spermatozoa.—A. I. Weisman found that pus obtained from the infected cervix did not exert any inhibitory effect on the survival of spermatozoa *in vitro*. It appeared indeed as though pus and necrotic material actually prolonged spermatozoal mobility. The author considers that interference with spermatozoal mobility and migration could only be effected by pure mechanical obstruction due to impenetrable masses of thick purulent pus such as are found in acute infections. Thin pus offering no mechanical barrier does not provide any obstacle to spermatozoal migration.

Treatment

Tubal insufflation.—M. L. Leventhal and E. M. Solomon report that among 133 patients in whom the tubal patency test could be evaluated, 54, or 40.6 per cent, became gravid. In 114, or 85.7 per cent, of the patients in whom patency in one or both tubes was demonstrated, 51, or 45 per cent, conceived. In 19, or 14.3 per cent, of the patients in whom patency was not demonstrated to gas or oil, 3, or 15.8 per cent, conceived. Twenty-eight, or 21.5 per cent, patients became pregnant within 2 months of the test. Coitus immediately preceding the insufflation probably added to the high percentage of successes, and was not attended by ill effects.

Sterility in the Male

Diagnosis

Testicular biopsy.—C. W. Charny states that the performance of testicular biopsy before and after a given form of therapy of male infertility gives more direct evidence of the efficacy of that treatment than any other method in use at the present time. Though repeated examination of the semen gives evidence of the degree of progress as a result of treatment, it is not entirely accurate, because changes in the semen may occur as the result of factors unrelated to the process of spermatogenesis. Reduction in the sperm count may, for example, be caused by excessive coitus. On the other hand increased cellular activity in the seminiferous

Presence of spirochaetes in gastric mucosa

Associated with ulceration.—A. S. Freedberg and L. E. Barron examined gastric tissue from 35 patients who had undergone partial gastric resection, 19 for carcinoma, 14 for duodenal ulcer, and 2 for gastric ulcer. Of these 35 specimens, 13, or 37.1 per cent, contained spirochaetes. In all the patients the Wassermann and Kahn reactions of the blood were negative. The authors conclude that spirochaetes are often present in connexion with necrotic malignant or benign ulceration, but are rare in the absence of ulceration.

Depressant effect of carcinoma extracts on gastric secretion

A. Brunschwig, T. H. Clarke, J. V. Prohaska, and R. Schmitz found that boiling water or 0.2 per cent hydrochloric acid extracts of the mucosae and neoplasms of achlorhydric carcinomatous stomachs, when neutralized and injected intravenously in dogs with stimulated gastric pouches, resulted in a marked depression of pouch section and achlorhydria with 11 (50 per cent) of 22 extracts studied. Similar depressant effects were noted with 14, or 19 per cent, of 73 extracts of stomachs without benign or malignant growths.

Course and prognosis

Termination by Lederer's acute haemolytic anaemia.—J. M. Holmes and A. J. McCall report cases of primary carcinoma of the stomach, with wide-spread metastases. The patients were a woman aged 49 and a man aged 26. Necropsies were performed on both cases; in the first case the bone marrow of the femur, humerus, and lumbar vertebrae showed carcinomatous infiltration which was not proved to be present in the second case, the examination in the case not being so complete. The blood picture was that of leuco-erythroblastic anaemia, resembling clinically Lederer's acute haemolytic anaemia. That the jaundice was haemolytic or, as A. R. Rich preferred to call it, *retention jaundice*, is in the authors' opinion possible, but not satisfactorily proved in these cases.

Diagnosis and differential diagnosis

Tuberculous ulcers.—A. E. Connolly records a case of tuberculous ulcers in the stomach of a woman, aged 45, with a history of anorexia, epigastric pain, loss of weight, and weakness. There was a hard mass in the epigastrium, the faeces gave a positive reaction for occult blood, and a fractional test meal disclosed free acid in the stomach. The sputum was negative for tubercle bacilli, and radiologically the lungs were normal. The clinical and radiological evidence pointed to carcinoma of the stomach. At the necropsy the lungs were free from tuberculosis, the intestines showed many adhesions, numerous caseous nodules and glands, a fistula between the transverse colon and the small intestine, and 5 ulcers about the middle of the lesser curvature of the stomach, $\frac{1}{2}$ to $\frac{3}{4}$ inch in diameter, the floor of the ulcers showing caseous material and tubercle bacilli. Near the pylorus there were two small caseous nodules which had not reached the stage of ulceration between the peritoneal and muscular coats, and caseating glands in the neighbourhood but not closely connected with the stomach. A review of the recorded cases brings out the difficulty of the accurate diagnosis, especially from ordinary gastric ulcer and from carcinoma. A. C. Broders from collected data concluded that about half the cases so described were doubtful or erroneous. A 'false' form of pyloric obstruction, due to tuberculous lymphadenitis, has been described.

Treatment

Total gastrectomy and partial oesophagectomy.—J. M. Waugh and L. A. Giffin record a case in a man, 72 years 2 months and 17 days old, who for 7 or 8 years had suffered from loss of appetite and nausea, but not vomiting, after food, and had recently lost 7 or 8 pounds. Radiologically there was extensive carcinoma of the cardiac end of the stomach with involvement of the terminal portion of the oesophagus; there was obstruction at the lower end of the oesophagus with dilatation of the whole tube. At operation the carcinoma was seen to be limited to the cardiac end of the stomach and to surround the oesophagus and to invade it for about 1 centimetre. There were not any metastases visible on the surface of the liver. The whole stomach was removed with 1½ inches of the oesophagus, and several enlarged glands in the gastro-hepatic and gastro-colic ligaments were included in the resection. The duodenal stump was inverted and buried in the pancreas. The jejunum was brought anterior to the colon and attached to the oesophagus with one row of running silk sutures and two rows of interrupted silk sutures. The reflection of the oesophago-diaphragmatic peritoneum was sutured to the jejunum outside the site of anastomosis; this procedure protected the anastomosis from the tension which otherwise would be caused by the weight of the dependent limbs of the jejunum. Jejunum-jejunostomy was performed opposite the ligament of Treitz; a nasal tube was passed down into the distal jejunal limb beyond the anastomoses. There was an ulcerating, perforating adeno-carcinoma with extension through the wall of the stomach to the peritoneum, involvement of 2 regional lymphatic glands, and carcinomatous invasion under the mucosa of the oesophagus for a distance of about 1 centimetre. This case appears to be noteworthy (a) because it concerns the oldest patient to undergo successfully the operation of total gastrectomy, and (b) because the oesophagus was mobile and long enough to permit successful resection of the lower 1½ inches of the oesophagus; it suggests that in selected cases many patients with carcinoma involving the cardia and lower part of the oesophagus with oesophageal dilatation and obstruction, for whom operation has in the past been refused, may undergo this procedure with reasonable hope of success.

Total gastrectomy technique.—J. T. Priestley and K. C. Randall report the performance of total gastrectomy on a man, aged 31, who was in good condition, in spite of intermittent

epigastric pain and vomiting of 2 years' duration and loss of 50 pounds weight in the 3 months prior to examination. At operation there was an extensive diffuse colloid adeno-carcinoma, grade 4, with enlarged lymphatic glands along the greater and lesser curvatures; several of these contained colloid carcinoma, but one near the oesophagus did not. There was not any other obvious extension of the growth or of metastasis. As the lesion was relatively mobile, total gastrectomy was performed and an antecolic, oesophago-jejunal anastomosis established. The jejunum was anchored posteriorly to the capsule of the pancreas and anteriorly to the liver in order to prevent traction on the lines of suture to the oesophagus. An entero-anastomosis was made between the loops of the jejunum and a No. 20 F. catheter was placed in the distal loop of the jejunum, below the entero-anastomosis, for the purpose of feeding until after fluids were started by the mouth on the seventh post-operative day. A week later the jejunostomy tube was removed.

Diverticula of Stomach

Cardiac end

D. T. Bonham reports 3 cases of diverticulum of the cardiac end of the stomach. Two of these appeared to be false diverticula, or diverticula in which there was no break in the gastric wall due to disease, and the other appeared to be possibly congenital in origin. Removal of the sac in one case relieved all symptoms. The second patient, though untreated, remained free from symptoms for a year. The third patient remained free from symptoms while treated by postural drainage.

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STRABISMUS

See also B.E.M.P., Vol. XI, 492; Cumulative Supplement, Key No. 1465; and Surveys and Abstracts 1939, pp. 131 and 551; 1940, p. 546.

Treatment

Use of lacquered lenses

P. Good, discussing the use of lacquer applied to an ophthalmic lens to obscure vision, states that its advantages over the use of atropine in the fixing eye are: Distance and near vision are equally affected by the lacquer. There are no allergic reactions. The objectionable appearance of the dilated pupil is avoided. The amount of obscuration of sight can be controlled by the application of the lacquer. The advantages over a patch are: Binocular vision is stimulated, rather than suppressed. The lacquered lens is worn all the time, an important factor in the treatment of amblyopia. The field of vision is unimpaired, a fundamental point for safety when children are crossing roads. The disadvantage is that a child may do considerable peeping over the top of the lens at first. The degree of obscuration of sight due to the lacquered lens may be varied simply by the amount of stippling the lacquer receives as it dries. Lacquer will generally adhere to the lens for about a month, during which time the lens may be washed in cold water. The author recommends this method in the treatment of squint, amblyopia, and diplopia.

Comitant (Concomitant) or Non-Paralytic Squint

Aetiology

Children.—B. F. Payne discusses the general aspects in children of squint, which is often inherited. Errors of refraction account for more than half of the cases, and inability to fuse the images of both eyes and to judge distances is common. Squint may be precipitated by psychological or physical disturbances, such as infections, but it is known that the latter are not in themselves a cause. Children with muscular imbalance find it difficult to read and judge distances, and suffer from headaches and eyestrain. Fusion and muscular co-ordination are difficult. Examination of every child before school age is recommended, including an estimate of the vision of each eye, examination of the eyelids, eye measurement using drops, interior examination for diseases, and the prescription of glasses and exercises if necessary. Surgery, though generally successful, should not be used until other remedies have been tried.

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Payne, B. F. (1941) *Arch. Pediat.*, **58**, 365.

SYPHILIS

See also B.E.M.P., Vol. XI, p. 526; Cumulative Supplement, Key No. 1467; Surveys and Abstracts 1939, pp. 151 and 553; 1940, pp. 87 and 547; and p. 102 of this volume.

Aetiology*Extragenital infection*

G. R. Rowntree and J. R. Hendon report an extraordinary series of cases of extragenital transmission of syphilis among 5 members of one family. A mother brought her baby, aged 18 months, to hospital because of a sore on the lower lip; this had appeared 6 to 8 weeks previously. Laboratory investigation led to a diagnosis of secondary syphilis with an extragenital primary source. An immediate examination of the entire family, including a boarder, made it clear that the child's mother, father, brothers aged 15, 8, and 4 respectively, and a boarder aged 23 were all non-syphilitic; a sister, aged 11 years, had a discharging indurated non-tender ulcer on the lower lip which had appeared about 3 weeks previously; a diagnosis of primary syphilis was made. Another brother, aged 6, had a fissured, encrusted lesion between the pinna of the left ear and the head, general enlargement of the lymphatic glands, and ham-coloured macules covering the body; he was found to have primary and secondary syphilis. Another sister, aged 17, had an excoriation on the mucous membrane of the lower lip, and enlargement of the cervical glands; the diagnosis was secondary syphilis. A brother, aged 19, was found to have early latent syphilis. A reconstruction of the history of these cases suggested that the brother, aged 19, had contracted the disease by kissing a girl friend who was found to have had treatment for syphilis. The other members of the family had received the infection from him through fondling.

Spread by sexual intercourse

Conjugal neurosyphilis.—Effie L. Hutton, working on the incidence of conjugal neurosyphilis, analysed the conjugal histories of 492 female neurosyphilitics. Her investigations indicate that conjugal syphilis only occurs if conjugal relations are established within a limited period after acquisition of syphilis by one of the conjugal partners; if the man acquired the disease first the period rarely, if ever, exceeds 2 to 5 years; if the woman, 1 to 2 years. The relatively small number of cases of conjugal syphilis (78) found by Hutton is in part because quite a large proportion of the conjugal relations began outside the period of contagion. The most striking feature in conjugal syphilis was the rarity of tertiary syphilis, as only 11 such cases were recorded, and of these 7 were cardiovascular and 1 showed leucoplakia. In contrast was the incidence of neurosyphilis, namely 38, with 2 cases of latent asymptomatic neurosyphilis, and 8 with probable neurosyphilitic syndromes. The percentage of syphilitics who became neurosyphilitics has been estimated by other authorities at 10 to 15 per cent, the conjugal incidence being considerably higher, thus lending support to the view that there is a neurotropic strain of the parasite. An important conclusion from these statistics is the rarity in conjugal neurosyphilis of both partners showing a simultaneous onset of neurosyphilitic manifestations; one usually succumbs months or even years before the other. Systematic inquiries and routine examination of the blood and, if necessary, of the cerebrospinal fluid, of the conjugal consorts of all patients with neurosyphilis would bring to light the existence of potential neurosyphilitics and enable prophylactic treatment to be undertaken, as has been carried out at Horton with good results.

Acquired Syphilis*Secondary*

Skin lesions resembling psoriasis.—M. J. Davis and R. H. Kampmeier report a case of secondary syphilis, in a youth aged 17, with generalized skin lesions resembling psoriasis. Spirochaetes were found in the lesions, which showed the characteristic clinical features of psoriasis. These lesions disappeared after 3 injections of arsphenamine.

Tertiary

Nodular syphilide of face.—L. S. Markson reports a case of tertiary nodular syphilide of the face in a man aged 32. The clinical diagnosis was confirmed by the history, then serologically, and finally therapeutically. The histological report, however, from a biopsy of a lesion on the right side of the nose suggested lupus vulgaris, because of the presence of epithelioid tubercles, and the absence of the usual microscopical appearance of a syphilitic process.

Congenital Syphilis*Clinical picture*

Incidence of heart disease.—According to Ruth A. Koons and R. W. Kissane, the relative incidence of heart disease in children with congenital syphilis closely approximates the incidence of congenital syphilis in known cardiac children. The incidence of heart disease in children with congenital syphilis is too low to justify consideration of syphilis as an aetiological factor in the production of congenital heart disease. The association of rheumatic heart disease and congenital heart disease is incidental.

Rhagades.—E. A. Strakosch and L. M. Nelson report 3 cases of post-rhagadic scars of congenital syphilis, and 1 case of non-syphilitic post-rhagadic scars. The scars of congenital syphilis are distinguished by diminution in the colour of the lip, by the partial loss of the muco-cutaneous border, and by the presence of linear furrows of the lip extending radially

into the surrounding skin. The lesions are in reality atrophy of the elastic tissue, and not true scars.

Unusual manifestations.—K. E. Landé reports 2 cases of congenital syphilis with unusual manifestations and pathology. In one, a baby several months old, there was a combination of severe congenital syphilis with a duodenal ulcer causing a fatal haemorrhage. The question arose whether the ulcer was of syphilitic origin. In the other case very advanced congenital syphilitic changes in the liver of a female baby twin, 5 weeks of age, were incompatible with further survival. The other twin did not show any signs or symptoms of syphilitic infection and, at the time of the report, was developing normally. Her serological blood reaction was, however, still positive.

Parrot's pseudo-paralysis.—T. M. Palmer reports 8 cases of Parrot's pseudo-paralysis. This clinical manifestation of congenital osseous syphilis consists of inability or definite disinclination to move one or more extremities. The pathological picture is that of osteochondritis, at times associated with true epiphysal separation, though there is generally diaphysal infraction. The author believes that the mechanism of the pseudo-paralysis is other than that of the bone lesion, since prompt return of function may follow even one dose of sulpharsphenamine, although X-rays show no improvement in the bone lesions. The bone lesions eventually disappear after continued arsenical treatment.

Treatment

Arsenical compounds

Acetylglycarsenobenzene.—W. H. Guy, B. A. Goldmann, G. P. Gannon, and J. Slone make a preliminary report on the use of acetylglycarsenobenzene (3:4'-diacetyl-amino-4-hydroxy-arsenobenzene-2' sodium glycolate) in the treatment of syphilis. The drug was given in the form of a sterile aqueous solution with 10 per cent glycerin and 0.005 gramme per cubic centimetre of ascorbic acid. Each cubic centimetre of the solution contains 0.07 gramme of the active constituent; in arsenic content (0.02 gramme) this is approximately equivalent to 0.1 gramme of neoarsphenamine. The solution was given by intramuscular injection. Eighty-four patients were treated. Regardless of the stage of the disease, the following routine was observed: A dose of the drug (6 cubic centimetres for male, and 4 cubic centimetres for female patients) was given once weekly for 6 weeks, followed by a weekly dose of an oil-soluble bismuth compound, 60 milligrams of bismuth, for 6 weeks, and 1 dose weekly (0.065 milligram of mercury) of mercury salicylate for 6 weeks. The therapeutic results obtained were approximately equivalent to the results reported with mapharsen. Although nitritoid reactions were not observed, the incidence of exfoliative dermatitis was much greater than with other known arsenicals. The authors conclude that, in view of the toxic reactions, the drug is not suitable for general use.

Acetarson.—According to J. Yampolsky, acetarson has a definite place in the treatment of congenital syphilis. In children under one year of age the use of acetarson will reverse the Kahn reaction in most cases, will heal the usual lesions of early syphilis, and will markedly improve the X-ray findings. In babies acetarson improves the appetite and increases the percentage of haemoglobin. The best results are obtained when bismuth is combined with acetarson; of 9 cases thus treated, 80 per cent showed a reversal of the Kahn test. Nearly all the clinical conditions improved or healed, and great healing or improvement was shown radiographically. The author considers that acetarson alone should be used in very young infants.

Effect of thiosulphate on excretion of arsenic.—M. R. Mattice, H. Baxt, and J. M. Byrne investigated the problem whether or not the administration of sodium thiosulphate assists the excretion of arsenic. They could not obtain any evidence that sodium thiosulphate given intravenously mobilized arsenic from body stores for urinary elimination; on the other hand, when an arsenical and a thiosulphate were injected within an hour of each other, in the order stated, the urinary excretion of the arsenic was much diminished. The administration of sodium thiosulphate for clinching the diagnosis of arsenical dermatitis is therefore not warranted.

Mapharside.—H. Gordon obtained 38 per cent permanently negative Wassermann reactions in less than 4 months by giving mapharside in divided doses in early cases of syphilis. This method appears to be less toxic than the continuous drip method. The lesions cleared up rapidly, the average length of stay in hospital being 8.5 days. The period of infectivity is much shortened. The technique was as follows: 5 injections daily of 0.02 gramme of mapharside, every 2 hours, were given for 5 days. Injections were given at 7 a.m., 9 a.m., 11 a.m., 1 p.m., 3 p.m., 4 p.m., 6 a.m., 8 a.m., 10 a.m., 12 noon, 2 p.m., and 3 p.m., 5 ounces of a 10 per cent solution of glucose were given by mouth. No other drug was given.

Bismuth

Elimination of tissue deposits by ammonium chloride.—E. F. Corson, H. B. Decker, and T. L. Williams gave ammonium chloride, in doses of 30 to 40 grains daily, to a group of patients who, by treatment records and X-ray observations, were shown to have deposits of bismuth in the tissues. Urinary tests for bismuth, which formerly gave negative results, gave positive reactions as a result of this therapy. When bismuth was not eliminated by this dosage, doubling the dose was in most cases promptly effective.

Mercury

Healing of obstructive lesions.—L. Tulipan considers that the formation of a dense fibrous

wall and obliteration of blood vessels in some tertiary syphilitic lesions prevents the entry of anti-syphilitic drugs administered parenterally. Mercury in the form of blue ointment (50 per cent metallic mercury) applied locally hastens the healing of such lesions.

Side effects of anti-syphilitic therapy

Petechial haemorrhages.—G. Horne and H. Scarborough state that spontaneous petechial haemorrhages are often associated with intolerance to anti-syphilitic therapy. Toxic manifestations of anti-syphilitic therapy are associated with a low or decreased capillary resistance which may precede the appearance of clinical signs and symptoms. These results suggest that the determination of capillary resistance might help to prevent the occurrence of intolerance during anti-syphilitic and other forms of therapy with heavy metals.

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TESTIS AND CORD DISEASES

See also B.E.M.P., Vol. XI, p. 656; and Surveys and Abstracts 1939, p. 559; 1940, p. 550.

Tumours

Aetiology

Seminoma of an abdominal testis.—M. J. Bennett-Jones and C. V. Harrison report the case of a man, aged 55, with a seminoma of an abdominal testis, and also a glioma in the right frontal lobe of the cerebrum. The case is of interest in connexion with primary malignant disease in an undescended testis. The authors consider that the removal of a unilateral undescended testis which cannot be fixed in the scrotum is justifiable, especially after puberty, because the organ is unduly liable to malignancy, and, further, there is not any risk of hormonal deficiency from its removal.

Clinical picture course

Concurrent seminoma and teratoma.—J. R. McDonald and A. C. Broders report a case of seminoma and teratoma occurring in the same testis of a patient aged 27 years. Most of the few reports of seminomas and teratomas in the same testis have been concerned with men less than 35 years old. The authors conclude that the two neoplasms had a separate histogenesis.

Traumatic displacement of testis resulting in seminoma.—A. Pytel records a case of a boy who when 12 years old jumped on a camel and received a serious blow on the scrotum, which was followed by disappearance of the right testis from the scrotum into the inguinal canal, where it remained in spite of efforts to return it back into the scrotum. Twenty-one years later the testis was noticed to be enlarged and was removed with a hydrocele, being then six times its normal size and occupied by a seminoma. Reference is made to 25 reported cases of traumatic displacement of the testis, 23 having been collected in 1929 by E. P. Alyea from records made in 130 years (1800–1929). Malignant disease of a testis among such cases is very rare. That malignant disease may supervene in ordinary retained testis has long been recognized.

Interstitial celled tumour and precocity.—Anne E. Somerford reports a case of interstitial celled tumour of the testis in a boy aged 11. For 6 years there had been a gradual painless enlargement of the right side of the scrotum, associated with precocious development. There was pubic hair, and the boy had the muscular development of a youth of 18. After removal of the tumour the boy was kept under observation for 18 months, but the secondary sexual characters did not show any sign of regression.

Bilharziasis of the testis.—M. Gelfand and G. B. Davis report a case of bilharziasis of the testis. In most cases the patient presents enlargement of the testis. There is often an accompanying hydrocele. The testis, although finely nodular, so closely resembles a carcinoma that it is practically impossible to distinguish it from the latter. Pathologically the testis has a characteristic appearance. Microscopically it often shows small whitish conglomerate nodules like sago grains, overgrowth of connective tissue being prominent. On section, the testis is

gritty, from calcified ova, and histologically there are foci or nodules scattered throughout the testis. In some cases the presence of ova in the urine or stools may suggest the diagnosis.

Treatment

Final results of injection treatment.—G. H. Ewell, C. R. Marquardt, and J. C. Sargent report on the final results of the injection treatment of hydrocele, and find that out of 165 cases followed up there were 7, or 4·3 per cent, of recurrences; this is approximately the same rate of recurrence after operation. They conclude that injection with quinine-hydrochloride and urethane is safe and effective, and in the vast majority of cases is the method of choice.

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McDonald, J. R., and Broders, A. C. (1941) *Amer. J. Clin. Path.*, **11**, 138.

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TESTIS, UNDESCENDED

See also B.E.M.P., Vol. XI, p. 671; Cumulative Supplement, Key No. 1480; Surveys and Abstracts 1939, p. 561; 1940, pp. 14 and 551; and p. 5 of this volume.

Treatment

Gonadotrophic hormones

There has been much controversy about the value of endocrine treatment of undescended testis. R. H. Kunstadter, during the past 8 years, treated 71 cases by gonadotrophic hormone; of these 65 had not received any other treatment, whereas 6 had been subjected to surgery. In the former group, complete descent occurred in 45, or 69·2 per cent, partial descent in 7, or 10·8 per cent, and complete failure in 13, or 20 per cent. Eighteen of the cases were unilateral and 47 were bilateral. Most of the failures in treatment were in unilateral cases which showed no definite evidence of endocrine disturbance. Three of these patients, in whom surgery had been a failure, responded to endocrine treatment. Unfavourable reactions were usually minor in character, and treatment was discontinued only on two occasions because of unpleasant experiences. When failure of endocrine treatment appeared to be inevitable, injections were discontinued and immediate surgical treatment recommended. The response of endocrine treatment generally occurred with a total dosage of 2,500 to 7,200 rat units of chorionic gonadotrophin and from 240 to 2,550 units of equine gonadotrophin. Undescended testis should be treated between 8 and 12 years of age, and disagreement is expressed with the view that it is safe to wait until after puberty so that nature may take its course. A high percentage of testes, undescended at puberty, are sterile. All boys with this condition should be given the benefit of a trial of endocrine treatment when no obvious surgical condition, such as hernia, exists.

Chorionic gonadotrophic hormone and testosterone propionate.—C. Zelson and E. Steinitz employed combined treatment with chorionic gonadotrophic hormone and testosterone propionate in 17 boys with cryptorchidism, 2 being bilateral. Four of the patients received injections of 500 rat units (1 rat unit is approximately equal to 1 international unit) of gonadotrophic hormone with 5 or 10 milligrams of testosterone propionate, given intramuscularly, 3 times a week, and 13 received 500 rat units of gonadotrophic hormone and 10 milligrams of testosterone propionate, 3 times a week. Treatment lasted from 3 to 12 weeks. The total dosage of gonadotrophic hormone ranged from 4,000 to 14,500 rat units, and of testosterone from 40 to 270 milligrams. Complete descent occurred in nine, or 53 per cent of the cases, and there was not any effect on the other 8. Nine of the children received previous treatment with either hormone alone or successively without success, and of these 4, or 44 per cent, were among the successful cases.

Surgical and hormonal treatment

Indications.—J. S. Eisenstaedt, M. Appel, and M. Fraenkel state that the group of abnormally situated testes which will invariably descend when they reach or approach adult size and weight are to be differentiated clinically from the group of true undescended and ectopic testes. True undescended and ectopic testes always require operative treatment, whereas retractile testes may descend spontaneously as late as the seventeenth year. The authors believe that gonadotrophic substance has no value in the pre-operative care of true undescended and ectopic testes, and its routine use is not recommended. In larger doses it is definitely harmful to testes which have not reached the scrotum.

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TETANUS

See also B.E.M.P., Vol. XII, p. 1; Cumulative Supplement, Key No. 1481; and Surveys and Abstracts 1939, p. 562; 1940, pp. 10, 137, and 552.

Treatment*Prophylactic*

Combined immunization against tetanus and enteric fever.—J. H. Maclean and L. B. Holt found that the simplest effective method of simultaneous immunization against tetanus and enteric fever was the administration of 2 doses of the combined antigens at an interval of 4 weeks. The response to the antigens of the T.A.B. vaccine was as good as if these were administered at the usual short interval of 1 week. The amount of the tetanus antitoxin in the serum of the immunized men was more than 5 times as great as it was in those who had 2 doses of tetanus toxoid alone at intervals of 4 or 6 weeks. In every subject tested it was found that there was an antitoxic titre of over 1 unit of antitoxin per cubic centimetre in the patient's serum, which is much higher than that which is accepted as an immunizing level against tetanus. In 50 per cent of cases the antitoxic titre rose to 5 units or more per cubic centimetre, which is many times higher than would be reached by the usual prophylactic dose of tetanus antitoxin. The reaction to the combined antigens was no greater than to T.A.B. vaccine alone. The first injection contained *B. typhosum*, 500 millions, *B. paratyphosum A*, 250 millions, *B. paratyphosum B*, 250 millions, tetanus toxoid, 0.9 cubic centimetre; and the second contained *B. typhosum*, 1,000 millions, *B. paratyphosum A*, 500 millions, *B. paratyphosum B*, 500 millions, and tetanus toxoid, 0.9 cubic centimetre.

Tetanus toxoid.—D. M. Marvell and H. J. Parish found that 2 doses of tetanus toxoid, at an interval of 6 weeks, induce useful amounts of circulating antitoxin. Spacing of the doses at intervals greater than 6 weeks gives better immunity. A third injection of 1 cubic centimetre given after a long interval, e.g. 7 to 9 months, often produces a dramatic increase in circulating antitoxin, and more than counteracts any tendency of titres to drop below levels which might be considered safe.

Curative

Sedation, antitoxin and hexamine.—H. I. Vener and A. G. Bower treated consecutively 100 patients with tetanus giving a mortality rate of 29 per cent as compared with 56.5 per cent in previous years. If the patients dying during the first 24 hours are excluded, the net mortality rate was 19.3 per cent among 88 patients. The method of treatment was as follows: sedation, local treatment of the wound, antitoxin therapy consisting of 20,000 units given locally, 60,000 units given intramuscularly, 20,000 units cisternally, and 40,000 units intravenously in saline, an intravenous dose of 20,000 units being repeated in 3 hours, in the absence of any reaction; and 40,000 units intramuscularly proximal to the previous site of injection, making a total dose of 200,000 units within a period of 30 to 36 hours after admission to hospital. Hexamine, 15 grains (1 gramme), is also given intravenously 2 hours after the first intravenous dose of 40,000 units, and 10 to 12 hours after each of the large intramuscular doses of antitoxin.

Intracisternal injection of antitoxin.—W. M. Firor showed that the intracisternal injection of tetanus antitoxin in dogs with early, mild, or moderately severe tetanus gave much better results than those of intravenous injection. In animals with severe tetanus there was little difference in the results obtained from the various routes of administration of antitoxin, but the difference which occurred was in favour of the intracisternal route.

Sulphapyridine and evipan sodium.—J. Bryant and H. D. Fairman treated 22 patients with tetanus by sulphapyridine and by continuous or intermittent narcosis with evipan sodium (soluble hexobarbitone). Of these patients only 5 died. Tetanus supervened in 6 cases after infection with guinea worm, although the guinea worm infection may have been purely incidental. The evipan sodium was injected in doses of 1 gramme night and morning, with, if necessary, 1 gramme at midday. Great relief and muscular rest resulted. Narcosis was prolonged, if necessary, by the use of morphine or other sedatives. Sulphapyridine was injected in doses of 1 tablet, 0.5 grain, suspended in 5–10 cubic centimetres of saline. As many as 3 to 5 intramuscular injections of 1.5 to 2.5 grammes of the drug were given. The authors believe that, when serum is unobtainable, this treatment may be of great value.

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THROMBOSIS OF CEREBRAL VEINS AND SINUSES

See also B.E.M.P., Vol. XII, p. 17; and p. 92 of this volume.

Aetiology*Primary thrombosis*

Puerperal.—J. Purdon Martin and H. L. Sheehan record 5 cases of primary thrombosis of cerebral veins occurring after childbirth, and 1 after typhoid fever with epileptiform attacks followed by word-blindness and impairment of postural sense. Three of the 5 cases were seen at necropsy and one at an exploratory operation. W. R. Gowers classified as *primary* thrombosis of the cerebral veins those due to the state of the blood and circulation generally and not consequent on disease near the brain or venous sinuses. Martin and Sheehan consider

that thrombosis of the cerebral veins is not very rare. In the past the puerperal cases have often been regarded as examples of 'late eclampsia' or cerebral embolism. The outstanding clinical features are fits and paralyses; the fits may be local or general, and occasionally are absent. It is suggested that when the condition is recognized, heparin might be tried in order to prevent spread of the thrombosis.

Treatment

Staphylococcal cavernous sinus thrombophlebitis

Heparin and sulphonamide therapy.—C. Lyons reports the successful treatment of 2 consecutive cases of bacteraemic staphylococcal cavernous sinus thrombophlebitis of the anterior type by a combination of heparin and sulphonamide. In one case a total of 225,000 units of heparin, and in the other 580,000 units were employed. Sulphathiazole was given in a dosage sufficient to maintain the blood level at 5 milligrams per 100 cubic centimetres.

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TONSIL DISEASES

See also B.E.M.P., Vol. XII, p. 40; Surveys and Abstracts 1939, p. 563; 1940, p. 553; and p. 60 of this volume.

Chronic Tonsillitis

Tuberculous infection

E. Rosencrantz and S. Hurwitz report that 18 per cent of 103 female tuberculous children had tuberculosis of the tonsils. The tuberculous process in the tonsils was latent and there was not any macroscopical change apparent, the condition being found microscopically. Of the 19 patients with tonsillar tuberculosis 18 showed tubercle bacilli in the gastric contents as revealed by guinea-pig inoculation.

Rosencrantz, E., and Hurwitz, S. (1941) *Amer. Rev. Tuberc.*, 43, 388.

TOXICOLOGY: HOMICIDAL, SUICIDAL, AND ACCIDENTAL POISONING

See also B.E.M.P., Vol. XII, p. 59; Cumulative Supplement, Key Nos. 1491–1527; and Surveys and Abstracts 1939, p. 565; 1940, p. 554.

Gases

Carbon monoxide

Mental and neurological sequelae.—Naomi Raskin and O. C. Mullaney observed the mental and neurological sequelae in a patient who survived accidental carbon monoxide asphyxia for 15 years. The patient became partially amnesic as regards the details of her past life, and showed diminished self-control, violent flare-ups of temper, secretiveness, religious fervour, and loss of sexual desire. Later the patient became sleepless and restless, the most annoying signs being chattering of the teeth, paraesthesias, difficulty of concentration, paraphasia, repetition of the same prayer, the same name, or even the same syllable, confusion, rhythmic picking at her clothes, tremors of left arm and leg, increased reflexes and bilateral ankle-clonus, thick mumbling speech, poverty of ideas, and rigid expressionless face with staring eyes. The morbid changes found at necropsy consisted of large bilateral symmetrical necrosis of the globus pallidus, miniature softenings, and small glial scars throughout the cortex, with corresponding areas of demyelination, mild vascular changes, and neuronal changes.

Corrosives

Acids

Sodium acid sulphate.—J. Beeman reports a case of poisoning by sodium acid sulphate. This substance is common in the home in the form of lavatory cleansers. In concentrated solutions the substance is highly corrosive, being in effect a half-neutralized sulphuric acid. In the case reported, the face, neck, and shoulders were burned a black colour. There was charring of the lower end of the oesophagus and of the gastric mucosa. Corrosion extended through the duodenum to the jejunum. There were not any other significant gross morbid changes.

Alkalis

Potassium salts and anuria.—A. W. Winkler, H. E. Hoff, and P. K. Smith state that cardiac death due to potassium absorbed from the gastro-intestinal tract can be produced experimentally in dogs by ligation of the ureters. The direct introduction of potassium salts into the stomach induces spasm of the pylorus, preventing absorption, and delaying death. Rapid death occurs when potassium salts are introduced directly into the duodenum of animals with ligated ureters. The authors conclude that poisoning from the oral administration of potassium salts is a distinct possibility in the presence of anuria from any cause.

Synthetic Organic Substances

Santonin

Fatal poisoning.—H. A. Cookson and C. J. H. Stock report a fatal case of santonin poisoning in a man of 21 years of age. He became violently sick and continued to vomit, off and on, for several days, when he passed into collapse. At necropsy the body showed great emaciation,

the oesophagus was whitened and blistered, and the stomach was greatly dilated and contained a small amount of milky fluid.

Acetanilide

Excess of headache powders.—T. N. Morgan and A. G. Anderson report a case of chronic acetanilide poisoning in a woman, aged 53, who had been taking powders containing the drug, 3 or more times a day, for headache. She was admitted to hospital on account of unexplained cyanosis. Laboratory investigation showed the presence of sulphaemoglobin-aemia, which, in the authors' opinion fully explained the cyanosis, without assuming the existence of a coloured derivative of aniline as suggested by E. Lundsteen, E. Meulengracht, and A. Rischel, who recorded 11 cases of poisoning due to acetanilide.

Barbiturates

Dilantin sodium.—H. Mandelbaum and L. J. Kane report a case of dilantin sodium (sodium diphenylhydantoinate) poisoning in a woman aged 34. After having taken a total of 58½ grains of the drug, she noted on the body a faint rash which disappeared. When a total of 114 grains had been taken she complained of weakness, headache, and a general burning sensation. A morbilliform rash appeared, and spread over the whole body. The temperature rose to 105° F. The dermatitis became more severe and exfoliative. The liver and spleen became much enlarged. A recrudescence occurred 5 days after an apparent recovery.

Antidotes.—J. P. Anderson reviews 20 cases of attempted suicide by barbiturate poisoning, in 19 of which picrotoxin was employed as an antidote. Of these, 15 patients recovered. The author found that serious poisoning does not occur unless approximately twelve times the usual dose of the drug is taken. Picrotoxin was found to be effective and no harmful effects followed its use. The drug should be given in sufficient dosage to keep the patient in a slightly restless condition and he should not be allowed to lapse into deep coma. An important part of treatment is prompt lavage of the stomach, after which the injection of glucose and sodium chloride solution should be given.

Oil of wintergreen

Fatal poisoning.—W. T. Shirreff and L. N. Pearlman report 2 cases of oil of wintergreen poisoning, ending fatally. Vomiting occurs early, and is followed by rapid respirations, generally about 6 hours after taking the poison. Thirst is common. Convulsions, stupor, drowsiness, and coma have been noted. Cyanosis, tinnitus, and dimness of vision occur. The urine gives a positive ferric chloride test to salicylates. Ketonuria is generally present. Blood changes give evidence of impaired renal function; there is increase of non-protein nitrogen, chlorides, and phosphates. The blood-sugar may be raised. The carbon dioxide-combining power of the blood is generally reduced, although this may not occur.

Alkaloids

Atropine group

Unusual features.—A. B. Carter reports accidental atropine poisoning with some unusual features, in a previously healthy man of 73. The accepted teaching is that susceptibility to atropine increases with age, but in this case recovery occurred after taking 5 drachms of belladonna liniment, the equivalent of 1·2 grains of atropine alkaloid. A further unusual feature is that treatment was not begun until 10 hours after the drug was taken. Further unusual features were noted in the symptoms, namely, increased spasticity in the limbs with an extensor plantar response on one side for a short time, and profuse sweating. Treatment consisted of the administration of morphine and physostigmine, and lumbar puncture to control the convulsive movements.

Nicotine

Effect on normal and damaged hearts.—S. Bellet, A. Kershbaum, R. H. Meade, and L. Schwartz carried out experiments in normal animals and in animals in various stages of myocardial infarction after coronary ligation to study the cardiac effects resulting from the inhalation of tobacco smoke and nicotine injection. It was found that normal unanaesthetized animals were able to tolerate a fairly wide range of dosage with the production of only slight electro-cardiographic changes. As a result of myocardial damage produced by coronary ligation, considerable electro-cardiographical changes occurred with a dose that was one-fourth of that required to produce only slight changes in the normal animal. These changes became less emphasized as the subacute stage was reached, and were still less evident in the chronic stage of infarction. The factor of tolerance was considered and shown not to influence materially these results.

Fatal poisoning in a child.—R. W. Cragg and A. E. Osterberg record a fatal case of nicotine poisoning, probably by swallowing snuff, in a boy aged 4½ years, and review the subject of acute nicotine poisoning. After the onset of acute nausea and vomiting the boy improved slightly for about 20 hours when he was seized by generalized tonic convulsions, respirations being first very rapid and then ceasing entirely, death supervening 20 minutes after the onset of the convulsions. Necropsy 1½ hours after death showed considerable dilatation of the cardiac ventricles, ascribed to the asphyxial mode of death. The stomach contained 30 cubic centimetres of thick yellow liquid and the mucosa was covered by a thick, yellowish-white coating which could be scraped off only with difficulty. Histologically the gastric wall showed severe inflammation; the specific secretory mucosal cells were almost completely absent and their place taken by masses of lymphocytes, reticular and fibrous tissue cells. The surface of the mucosa was frankly necrotic and covered by much fibrin. Chemical examination of the

stomach and its contents showed absence of strychnine. As part of the gastric extract gave a faint smell of tobacco, it was tested for nicotine with a positive result. It was later learned that the boy had had access to snuff. Acute fatal nicotine poisoning is rare and snuff is said to be the form of tobacco most seldom responsible. H. W. Willis (1937) could find 9 cases only in children.

Inorganic and Metallic

Arsenic

Vitamin B therapy in arsenical peripheral neuritis.—R. W. Vilter, C. D. Aring, and T. D. Spies employed synthetic vitamin B₆ and α -tocopherol in a severe case of arsenical peripheral neuritis. The patient had previously been treated with 50 milligrams of thiamine hydrochloride without effect. He was then given 50 milligrams of α -tocopherol intramuscularly, twice daily for a week, with no improvement. Then 20 milligrams of synthetic vitamin B₆ in sterile physiological saline were given intravenously twice daily for 3 days. During this period there was a striking increase in strength, and a decrease in hyperaesthesia, deep pain, and cramping sensations. A relapse occurred on three occasions when vitamin B₆ was discontinued. The most spectacular remissions occurred when vitamin B₆ and α -tocopherol were given together. To maintain the improvement these substances had to be given daily.

Cerebral symptoms.—A. D. Ecker and J. W. Kernohan state that well recognized chronic arsenical poisoning is often manifested by diffuse cerebral symptoms, such as fatigue, headache, vertigo, drowsiness, and impaired mental activity. The toxic effect of arsenic on the nervous system is not specific, and is marked by alterations in the ganglion cells and by regions of perivascular necrosis. In subacute and chronic forms these necrosed areas become filled with lymphocytes and plasma cells.

Bismuth

Anuria in infants.—S. J. McClendon reports the cases of a boy, aged 2 years, and of a girl, aged 15 months, in whom toxic effects resulted from a single injection of a bismuth preparation. The boy had received an intramuscular injection of 0.2 gramme of a bismuth preparation, and the girl had been given 0.15 gramme. Both children were acutely ill, and were completely anuric for about 24 hours. The author lays stress on the need for care in the administration of bismuth to patients with acute infections which usually respond readily to other treatment, and that this metal should be cautiously used in all children. The urine should always be watched carefully during treatment with bismuth, and any deviation from normal should be a signal for the discontinuance of the drug.

I. J. Zimmerman reports a case of anuria in an infant, which was presumably caused by the cumulative action of injected bismuth superimposed on a chronic pyelonephritis, and relieved by bilateral decapsulation of the kidneys. In this case there were considerable oedema and congestion of the kidneys. The infant made a good recovery after the operation.

Hydrogen sulphide

Poisoning during permanent wave.—A. H. Bunce, F. P. Parker, and G. T. Lewis (1941) report a case of accidental death from the absorption of heat-less permanent-wave solution. The patient died while the permanent wave was being made. Necropsy showed extreme congestion of the liver with possible degeneration, splenomegaly with degenerative change, severe congestion of the kidneys, extreme cerebral oedema, some abnormality of the blood, examination of which strongly suggested that the waving solution had been absorbed, and that the absorbent substance was either hydrogen sulphide or ammonium sulphide, and multiple areas of complete destruction of the stratified squamous epithelium of the scalp. The clinical course of the patient at the time of death and the pathological changes found at necropsy were identical with those occurring in reported cases of acute hydrogen sulphide poisoning.

Selenium

In endemic areas.—M. I. Smith states that, although human poisoning, in selenium endemic areas, from the ingestion of naturally occurring seleniferous foodstuffs has not been definitely established, the evidence of absorption of selenium in man in such areas, sometimes in amounts sufficient to cause harmful effects in experimental animals, appears to be conclusive. The positive diagnosis of chronic endemic selenium poisoning in man presents difficulties.

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TOXICOLOGY: INDUSTRIAL POISONING

See also B.E.M.P., Vol. XII, p. 127; Cumulative Supplement, Key Nos. 1528-1540; and Surveys and Abstracts 1939, p. 570; 1940, p. 559.

Mercury

Organic mercury compounds

In manufacture of fungicidal dusts.—D. Hunter, R. R. Bomford, and D. S. Russell report 4 cases of poisoning from the inhalation of methyl mercury compounds in a factory in which fungicidal dusts were manufactured without the use of a completely enclosed apparatus. Except for tremor, the symptoms of poisoning by inorganic mercury were absent, and the nervous system alone was affected. In all cases severe generalized ataxia, dysarthria, and gross constriction of the visual fields were present, and in 2 cases one or both plantar responses were extensor. Memory and intelligence were unaffected. Experiments on rats and a monkey showed that methyl mercury iodide and nitrate affect selectively certain parts of the nervous system. In rats the peripheral nerves and posterior spinal roots are affected first, and the posterior columns and the granular layer of the middle lobe of the cerebellum later.

Benzene and its Homologues

Effect on printer

L. J. Goldwater and M. P. Tewksbury describe surveys of benzene poisoning among three groups of printing workers made 2, 14, and 24 months respectively after the use of benzene had been suspended. Fifty-six men examined after 2 months showed persistent poisoning. A small minority of 49 men examined after 14 months were still affected and 4 out of 108 men examined after 2 years were still abnormal. As an index of recovery haemoglobin values, erythrocyte and platelet counts were taken. The mean corpuscular volume was also taken, as benzene poisoning induces an enlarged size of the erythrocytes. Leucocyte counts and lymphocyte percentage counts are thought to be unreliable indications of recovery. Anti-anaemic treatment was given but was not effective in speeding up recovery. It does not appear probable that benzene substitutes now in use contribute to the delay in recovery.

Diagnosis and differential diagnosis of chronic benzene poisoning

J. L. Hamilton-Paterson, in a report on 3 cases of chronic benzene poisoning, states that the diagnosis of benzene poisoning may be missed, if the occupational history is not investigated, and if only one type of blood picture is looked for. The blood may show either anaemia or polycythaemia, leucopenia or leucocytosis, a relative decrease or increase of polymorphs, and eosinophilia. The commonest findings, however, are leucopenia and anaemia. Any menstrual disturbance is suggestive. The ratio of inorganic to organic urinary sulphates is decreased. Urinary sulphate estimation is valuable during, and up to a month after, the period of exposure to benzene. Residual changes in the blood picture may persist indefinitely and may be accompanied by disability.

Carbon tetrachloride

Clinical picture.—E. M. Hammes, Jun. reports 2 cases of toxic effects in persons exposed to carbon tetrachloride in industry. In one case the exposure had continued for many years, whereas in the other an exposure of less than 4 hours caused symptoms. In one case there were severe symptoms of jaundice and oedema, and the liver was well below the level of the umbilicus, but there was not any evidence of renal dysfunction. In the other case the liver damage was less but there were manifestations of toxic nephritis.

Chlorinated Hydrocarbons

Methylchloride

Excreted porphyrins.—J. N. M. Chalmers, A. E. Gillam, and J. E. Kench report the occurrence of large amounts of porphyrins in the excreta in a case of industrial methylchloride poisoning. The effects of methylchloride poisoning appear to resemble those produced by certain nitro- and amino-compounds, as well as drugs of the sulphonamide group which probably act on the liver, interfering with the normal breakdown of haemoglobin.

Other Organic Compounds

Carbon disulphide fumes

Pathological changes in nervous system.—B. J. Alpers and F. H. Lewy record their experimental poisoning, by carbon disulphide fumes, of 9 dogs in connexion with the problem which not infrequently arises especially since the modern extensive use of carbon disulphide in the rayon industry, whether or not in a given case the clinical and pathological changes

are in fact due to that cause. A critical review of the subject is added. Very few reports of the lesions found in man are available, and of these 2 only seem of value; they showed changes in the cortical ganglion cells, chromatolysis and degenerations, degeneration of myelin sheaths in the brain, basal ganglia, and cord. Further, there were changes in the blood vessels and haemorrhages in the brain. In the dogs the lesions are more extensive in the cerebral cortex, basal ganglia, Purkinje cells, minor damage to the spinal cord, involvement of the peripheral nerves, and vascular changes are as constant but not so pronounced as those of the nervous elements. The authors conclude that the changes in the ganglion cells are not specific, but merely a manifestation of injury by a noxious agent. The difference in the human changes and in experimental dogs may be explained, at any rate in part, by the difference in length and degree of exposure to the chemical; the animals are subjected to a more concentrated dose of the gas than are human beings, whereas in men exposure is more prolonged, chronic, and sublethal than that of animals. This probably accounts for the more chronic type of cellular change in the human brain. In both man and animals there are extensive lesions in the basal ganglion system, and many patients show more or less complete evidence of Parkinsonism due to the changes in the extra-pyramidal system.

Alpers, B. J., and Lewy, F. H. (1940) *Arch. Neurol. Psychiat., Chicago*, **44**, 725.

Chalmers, J. N. M., Gillam, A. E., and Kench, J. E. (1940) *Lancet*, **2**, 806.

Goldwater, L. J., and Tewksbury, M. P. (1941) *J. industr. Hyg.*, **23**, 217.

Hamilton-Paterson, J. L. (1941) *Lancet*, **1**, 73.

Hammes, E. M., Jun. (1941) *J. industr. Hyg.*, **23**, 112.

Hunter, D., Bomford, R. R., and Russell, D. S. (1940) *Quart. J. Med.*, N.S., **9**, 193.

TRACHEA DISEASES

See also B.E.M.P., Vol. XII, p. 200; and Surveys and Abstracts 1939, p. 573; 1940, p. 563.

Inflammation

Tracheo-bronchitis

Treatment by sulphonamides.—Although sulphamethylthiazole and sulphathiazole may exert toxic effects, M. H. Shulman demonstrates, with 2 case reports, the efficacy of the drug in the treatment of staphylococcal tracheo-bronchitis. One patient was a girl of 2 and the other a 1-year-old boy. Both patients underwent tracheotomy, and pure cultures of *Staphylococcus aureus* were obtained from the trachea. The bacteria were also found in the blood and urine of one patient. Sulphamethylthiazole was given to the first patient, a Levine tube being used; it was kept at a blood level of 3–5 milligrams per 100 cubic centimetres and later discontinued slowly. The patient was discharged recovered on the twenty-third day since admission. The second patient was given sulphathiazole which reached a level of 30 milligrams per 100 cubic centimetres in the urine. It was gradually withdrawn and the patient having recovered was discharged 3 weeks after tracheotomy.

Shulman, M. H. (1941) *New Engl. J. Med.*, **224**, 978.

TRACHOMA

See also B.E.M.P., Vol. XII, p. 209; Cumulative Supplement, Key No. 1545; and Surveys and Abstracts 1939, p. 573; 1940, p. 563.

Treatment

Sulphonamide compounds

Sulphanilamide.—T. H. Luo and E. Chang report on the use of sulphanilamide orally in 40 cases of active trachoma. Thirty-two patients, or 80 per cent, were cured and 8, or 20 per cent, considerably improved. The average period of treatment necessary for a cure was approximately 3 months. In cases in which there was no cicatrix in the conjunctivae before treatment the trachoma became arrested with little or no scar formation.

Sulphanilamide, prontosil, and sulphapyridine.—O. S. Lee and H. Rottenstein report on the use of sulphanilamide, prontosil, and sulphapyridine orally in 75 cases of trachoma, and intramuscularly in 20 cases. By mouth the daily dose per pound of body weight was 0.02 gramme; treatment lasted from 2 to 4 weeks. By intramuscular injection, from 2 to 5 grammes of the drugs in a fine suspension in oil were given at intervals of 4 days in the case of sulphanilamide, and 7 to 10 days in the case of sulphapyridine. From 2 to 6 injections were necessary. The minimal therapeutic blood level proved to be between 2 and 2.5 milligrams per 100 cubic centimetres. The authors found that these drugs were definitely effective against trachoma in the first three stages, and were most useful in eliminating subjective complaints and in checking and healing pannus and corneal ulcer. Lesions in the palpebral conjunctiva were markedly improved, but always remained in the canthal regions. The upper and lower culs-de-sac were not much influenced by prolonged oral or intramuscular administration of the drugs.

Lee, O. S., and Rottenstein, H. (1940) *J. Amer. med. Ass.*, **115**, 107.

Luo, T. H., and Chang, E. (1940) *Chin. med. J.*, **58**, 512.

TRICHINIASIS

See also B.E.M.P., Vol. XII, p. 241; Cumulative Supplement, Key No. 1549; Surveys and Abstracts 1939, p. 575; and p. 90 of this volume.

Clinical Picture**Outbreaks in England**

J. E. S. Lee gives a clinical account of 7 cases of acute trichiniasis which occurred in the second half of December 1940 and the first half of January 1941, in the district of Wolverhampton. The clinical features of the cases were atypical and until laboratory evidence of trichiniasis was positive, caused difficulty in the differential diagnosis from nephritis, uraemia, pneumonia, enteric fever, and pyelitis. Another small outbreak, reported by L. P. Garrod and D. Maclean, occurred a month later in Hertfordshire. Four patients had eaten sausages within the fortnight before the onset of symptoms, but the source of the infested meat has not yet been established.

Trichinella Spiralis**Larvae**

Isolation from arterial blood.—G. J. Dammin reports a case of trichiniasis in which the larvae of *Trichinella spiralis* were recovered from arterial blood after unsuccessful examination of venous and capillary blood. The examination of arterial blood is suggested as a modification of the original technique of Herrick and Janeway.

Dammin, G. J. (1941) *New Engl. J. Med.*, **224**, 357.

Garrod, L. P., and Maclean, D. (1941) *Brit. med. J.*, **1**, 240.

Lee, J. E. S. (1941) *Brit. med. J.*, **1**, 237.

TROPICAL ULCER

See also B.E.M.P., Vol. XII, p. 256; and Surveys and Abstracts 1940, p. 565.

Treatment**Whale-oil application**

K. V. Earle recommends the use of whale oil, as an alternative to cod-liver oil, for local application in tropical ulcer, as an ointment consisting of whale oil 30 to 40 per cent, and vaseline 70 to 60 per cent. The ulcers are cleaned by several applications of copper sulphate solution, or by the use of magnesium sulphate and glycerin. The ointment is then applied and the lesion covered with elastoplast, which is left on for 10 to 14 days. The chief advantage of whale oil over cod-liver oil is that it does not give rise to an unpleasant odour.

Earle, K. V. (1941) *J. trop. Med. (Hyg.)*, **44**, 1.

TRYPANOSOMIASIS

See also B.E.M.P., Vol. XII, p. 263; Surveys and Abstracts 1939, p. 576; 1940, p. 78; and p. 100 of this volume.

Treatment**Curative**

4 : 4'-diamidinostilbene.—J. L. McLetchie reports on the use of 4 : 4'-diamidinostilbene in 14 cases of early Nigerian trypanosomiasis. Of these cases 8 were of a mild nature; these patients received a total dosage of 8.8 milligrams per kilo body weight, given in divided doses by intravenous injection on the first, third, fifth, seventh, and ninth days and by intramuscular injection on the eighth day. After 6 months, 7 of these patients were in good health; one had died after abortion. The second group of patients were in a more advanced stage of the disease; they reacted to intravenous injection of the drug and received an average of only 6.3 milligrams per kilo. They appeared to improve after treatment; but one died after 9 days, and after 6 months only 2 were really well, although symptoms appeared to be absent in all 5. After treatment with the drug no patient showed increase in the cell count or in the globulin content of the cerebrospinal fluid beyond that found initially, and four fluids, previously abnormal in some respect, had become normal. The strength of the drug employed was 100 milligrams dissolved in 10 cubic centimetres of distilled water. Toxic effects were slight, consisting of mild giddiness, salivation, nausea, precordial distress, and headache in some cases during intravenous injection. The author concludes that the drug appears to be as effective as Bayer 205 (suramin), but less effective than the combination of Bayer 205 and tryparsamide, in cases of trypanosomiasis without severe involvement of the nervous system.

R. D. Harding employed 4 : 4'-diamidinostilbene in 13 cases of trypanosomiasis; 3 mild or moderately severe cases were clinically cured and 1 improved, although in no instance did the cerebrospinal fluid, when initially pathological, return to normal. Of the other 9 moderate or severe cases one was clinically unchanged and 8 were definitely worse, but all showed greater disturbance of the cerebrospinal fluid after treatment followed by a varying period of observation. The author concludes that the results are not very encouraging.

Neocryl.—I. S. Acres reports a follow-up observation for 2 years of 21 cases of trypanosomiasis treated with neocryl (a succinyl derivative of *p*-arsamidic acid) in 1936–7. In first stage cases the results obtained compared favourably with those of tryparsamide. In patients in the second stage cases the results were disappointing, only 3 out of 12 cases being cured. These results compared very unfavourably with those treated in the same district and in the same year with tryparsamide. In 4 cases of relapse, a second full course of neocryl was given without result. Two of these patients did not respond to all later treatment with tryparsamide. Out of 8 relapsed patients treated with tryparsamide, 6 reacted favourably and 2 were

unresponsive. According to the authors it would appear that the trypanocidal activity of cerebrospinal fluid is less in those treated by neocryl than in that of tryparsamide.

Acres, I. S. (1940) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 281.

Harding, R. D. (1940) *Ann. trop. Med. Parasit.*, **34**, 101.

McLetchie, J. L. (1940) *Ann. trop. Med. Parasit.*, **34**, 73.

TUBERCULOSIS

See also B.E.M.P., Vol. XII, p. 286; Cumulative Supplement, Key No. 1554; Surveys and Abstracts 1939, pp. 39 and 577; 1940, pp. 94 and 566; and pp. 13 and 71 of this volume.

Epidemiology

Unsuspected carriers of Bacillus tuberculosis

J. Maxwell points out that the unsuspected carrier of *B. tuberculosis* is far more dangerous than the known carrier, for his existence may not be thought of until extensive damage has been done, and as far as the most careful clinical investigation can go, does not show any evidence of ever having been the subject of tuberculosis. In the light of the vast amount of work done on the carrier problem, comparatively little research has been devoted to the carriers of tubercle bacilli. The object of this paper is to point out that (1) apparently completely cured tuberculous subjects may still constitute a danger to the public health, and to suggest that (2) the disease may even be spread by contact with persons who appear to be perfectly normal; as the last mentioned is a difficult problem, four cases are reported in which there was not any evidence of tuberculous activity, and yet they were certainly infective from time to time. Complete reliance on a negative radiogram may in some instances be misleading; in such cases and in others a very diligent search for tubercle bacilli in the sputum should be carried out.

Immunity and Allergy

Susceptibility of red-haired persons

E. Bogen investigated 144 red-haired patients admitted to a sanatorium with tuberculosis, with the object of testing the statement that red-haired patients are more susceptible than others to tuberculous disease. He found that individual records often showed striking evidences of resistance to the infection and of the efficacy of collapse measures in its control. He concludes that such hypothetical susceptibility has not any confirmation in fact.

Prognosis

Grouping of cases

S. Cohen reviews 246 patients with fatal tuberculosis, and states that 45, or 18.3 per cent, showed clinical or radiological evidence of lymphatic or haematogenous spread of the disease during life. Of these cases 78 per cent were white and 22 per cent were coloured; negroes showed this dissemination about $2\frac{1}{2}$ times as often as whites. The ratio of males to females was about two to one. The author classifies the 45 cases into five groups as follows: (1) Miliary tuberculosis: in this group there were 7 patients with the acute or subacute types. All had negative sputa. There were 4 patients with the chronic type. The average duration of the illness in the acute type was 5 months and in the chronic type the duration was 2 to 12 years. (2) Subacute or chronic medium-sized nodular tuberculosis of which there was 1 case only. (3) Protracted multiform tuberculosis, of which there were 17 cases. The duration varied from 6 months to 9 years. (4) The transitional form of haematogenous pulmonary tuberculosis, of which there were 9 cases. The duration varied from 11 months to 12 years. (5) Pulmonary tuberculosis with extra-pulmonary haematogenous lesions, of which there were 16 examples with an average duration of $2\frac{1}{2}$ years.

Diagnosis

Blood viscosity

Pipette-type viscosimeter.—B. H. Y. T'ang and S. H. Wang describe a pipette-type viscosimeter which requires only about 1 cubic centimetre of plasma for the test, and gives measurements accurate up to the third decimal place, of the relative viscosity. The technique of plasma viscosity determination is much simpler than the blood sedimentation test, and can be completed within 15 minutes after the blood is drawn. The viscosity of the plasma is generally parallel with the activity of tuberculosis, and the viscosity value is often a more sensitive indication of the activity of tuberculosis than the sedimentation rate, especially in mild cases.

By flocculation test

W. H. McMenemy reports the results of the Meinicke flocculation test in 427 cases of tuberculosis and in 402 controls. With regard to established cases of tuberculosis, it was found that 21.3 per cent of tuberculous patients gave positive reactions and 23 per cent gave negative reactions. The tubercle bacilli + 1 positive patients gave 31 per cent positive and 10.3 per cent gave negative reactions; the TB + 2 patients gave 36.3 per cent positive and 23 per cent negative reactions. The TB + 3 patients gave 45 per cent positive and 10 per cent negative responses. Pleural fluids gave 44 per cent positive, 4 per cent negative reactions, and in 30 per cent of the patients the test failed to work. In a series of patients with non-pulmonary tuberculosis, 20.5 per cent gave positive and 29.5 per cent negative reactions. The author considers that the test is of little value in laboratory diagnosis.

Prevention

Effect of anthracite dust on tubercle bacilli

S. L. Cummins found that the addition of a small quantity of anthracite dust to quanta of living bovine tubercle bacilli, in 5 rabbits, led to their survival for considerably longer periods than the 5 control rabbits receiving bovine tubercle bacilli alone, and, in 1 rabbit, led to complete recovery up to 6 months. The author ascribes this to the absorption by anthracite dust of a proportion of toxic products of living tubercle bacilli in the tissues. This appears to bear out the belief that the inhalation of coal dust in coal-mines tends to prevent pulmonary tuberculosis.

Treatment

Various local lesions

Cod-liver oil.—A. L. Banyai reports on the local use of cod-liver oil in 270 cases of tuberculosis; pharyngeal and laryngeal ulcers showed rapid epithelialization and healing. Favourable results were observed in laryngeal tuberculosis with localized infiltration and with a vegetative granulation, but laryngeal tuberculosis with marked oedema was rather resistant to this treatment. Tuberculous empyema in the absence of broncho-pleural fistula responded favourably to aspiration of the pus and to its replacement by cod-liver oil. Suppurating tuberculous glands, when treated early, healed well on repeated aspirations followed by injection of cod-liver oil. Used in the form of eye-drops, cod-liver oil induced more rapid recoveries in phlyctenular conjunctivitis and kerato-conjunctivitis than other methods of treatment. The results were unsatisfactory in tuberculous keratitis. Cod-liver oil was of some value in cold abscess secondary to bone tuberculosis, and in fistulas originating from tuberculous epididymitis. The response in tuberculosis of the urinary bladder was disappointing, although there was some diminution in frequency and dysuria. Good results were obtained in most cases of ischio-rectal fistulas. Results were always good in scrofuloderma; 4 out of 5 patients with lupus vulgaris responded favourably to the local application of cod-liver oil.

Sulphapyridine

F. H. Heise and W. Steenken, Jun. report on the inhibitory effect of sulphapyridine on the growth of the tubercle bacillus in the test-tube and its effect on recent tuberculous infection in guinea-pigs. It was found that growth of tubercle bacilli on Smith and Steenken's and on Proskauer and Beck's media was not entirely inhibited by sulphapyridine even in concentrations of 80 milligrams per 100 cubic centimetres. Inhalation tuberculosis in guinea-pigs produced by relatively small doses was not inhibited by sulphapyridine in blood concentrations of 6.5 to 10 milligrams per cent after 5 months of treatment.

Vitamin C

M. M. Steinbach and S. J. Klein found that daily injections of vitamin C into tuberculous guinea-pigs appeared to increase the tolerance to repeated large doses of tuberculin and to retard the progress of tuberculosis. Fibrosis was more prevalent and caseation less prominent in animals which received vitamin C. The combined administration of tuberculin and ascorbic acid gave better results than the use of either substance alone. The best results were obtained in chronic tuberculosis. The authors suggest the use of ascorbic acid with tuberculin in man to minimize the toxic effect of the tuberculin.

Banyai, A. L. (1940) *Brit. J. Tuberc.*, **34**, 107.

Bogen, E. (1941) *Amer. Rev. Tuberc.*, **43**, 285.

Cohen, S. (1941) *Amer. Rev. Tuberc.*, **43**, 612.

Cummins, S. L. (1940) *Brit. med. J.*, **2**, 623.

Heise, F. H., and Steenken, W., Jun. (1940) *Amer. Rev. Tuberc.*, **42**, 801.

McMenemey, W. H. (1941) *Amer. Rev. Tuberc.*, **43**, 670.

Maxwell, J. (1941) *Brit. med. J.*, **1**, 665.

Steinbach, M. M., and Klein, S. J. (1941) *Amer. Rev. Tuberc.*, **43**, 403.

T'ang, B. H. Y., and Wang, S. H. (1941) *J. trop. Med. (Hyg.)*, **44**, 28.

TULARAEMIA

See also B.E.M.P., Vol. XII, p. 309; and Surveys and Abstracts 1939, p. 582; 1940, p. 569.

Bacteriology and Morbid Anatomy

Intracellular parasitism and Bacterium tularensis

According to E. W. Goodpasture, *Bacterium tularensis* apparently depends entirely upon an intracellular environment for growth in the living unaltered tissues and thus resembles *Brucella abortus*. The invaded host-cell seems to afford a stimulus or to supplement a deficiency in these parasites, of which advantage is readily taken. In the one case the intracellular parasitism is for the invader only an adventitious relation, in the other an advantageous one. This difference may be reflected in the relative difficulty of obtaining primary cultures of *B. tularensis* on artificial media, as compared with the easy adaptability of *Pasteurella pestis* to similar *in vitro* conditions. *B. tularensis* is essentially an intracellular parasite and is therefore unlikely to respond to sulphonamide drugs. (See also sulphonamide drugs and intracellular parasites.)

Aetiology

Infected animals

Diagnosis from meningitis.—J. H. Tillisch records a case of a farmer, 29 years of age, who

had been tentatively regarded as suffering from meningitis because of agonizing headache, photophobia, some rigidity of the neck, and fever. Positive agglutination of *Pasteurella tularensis* did not appear until the twenty-fifth day of illness. It is pointed out that E. Francis, in reporting 24 fatal cases of tularaemia, found 5 that appeared to be meningitic. The only source of infection in the farmer was the cat; later it was found out that a kitten which had scratched him had fed on dead rabbits. Among 28 cases of the typhoid form of tularaemia, W. M. Simpson found that 20 were among laboratory workers who had performed necropsies on infected animals or had handled infected ticks.

Francis, E. (1928) *J. Amer. med. Ass.*, **91**, 1155.

Goodpasture, E. W. (1941) *Trans. Studies Coll. Phys. Phila.*, 4 ser., **9**, 1.

Simpson, W. M. (1929) *Tularemia, History, Pathology, etc.*, New York, 89.

Tillisch, J. H. (1941) *Proc. Mayo Clin.*, **16**, 205.

TUMOURS

See also B.E.M.P., Vol. XII, p. 313; and Surveys and Abstracts 1939, p. 583; 1940, p. 569.

Morbid Anatomy

Microscopic features

Effect of irradiation on mitosis.—I. Lasnitzski, carrying on work previously undertaken at the Strangeways Research Laboratory, Cambridge, found that irradiation causes within 80 minutes a fall of mitosis in cells cultivated *in vitro*. This is followed by an attempt at recovery in cell division, accompanied by an appearance of degenerate cells. Degeneration of cells occurring within 24 hours of exposure to X-rays is mainly due to the breaking down of cells that have undergone early changes in the nucleus to the appearance of discrete chromosomes, a phase known as prophase. These changes closely resemble those seen in experiments *in vivo*. The effect of irradiation is independent of any effect on blood circulation.

Multinucleosis among Bantus.—J. Gillman reports on the occurrence in the Bantus in Johannesburg of bi-nucleated and multi-nucleated cells in the highly specialized tissues. This is described as a distinctive feature in organs free from disease among the Bantus. It occurs especially in the liver, 20 per cent, in the stomach, 6 per cent, pancreas, 5·5 per cent, pituitary and other organs, but is remarkably rare in the intestine. The nature of these changes is discussed: bi-nucleosis and multi-nucleosis may or may not be associated with evidence of cellular degeneration; fusion of cells is regarded as improbable, and 800 bi-nucleated or multi-nucleated cells were examined without the detection of changes suggesting the mitotic origin of twin nuclei. It has not been possible to determine if bi-nucleosis is as common in Europeans as it is in Bantus. The high incidence of bi-nucleated cells in the liver of Bantus is of interest in connexion with the high incidence of primary carcinoma of the liver in male Bantus (see abstract, pp. 289 and 290), but this point is hardly mentioned by the author.

Gillman, J. (1940) *S. Afr. J. med. Sci.*, **5**, 46.

Lasnitzski, I. (1940) *Brit. J. Radiol.*, **13**, 279.

TYPHUS FEVERS

See also B.E.M.P., Vol. XII, p. 325; Cumulative Supplement, Key Nos. 1558–1560; Surveys and Abstracts 1939, p. 583; 1940, pp. 76 and 570; and p. 98 of this volume.

Epidemic or Louse-Borne Typhus Fever

Treatment

Preventive: Mexican murine vaccination.—M. H. Finlayson and G. M. Grobler found that guinea-pigs immunized with Zinsser-Castaneda vaccine prepared from a Mexican murine typhus strain were immune to subsequent infection with South African epidemic typhus. The degree of immunity produced varies directly with the number of injections of vaccine given at weekly intervals. Three doses of the vaccine given at weekly intervals produce a high degree of immunity which lasts for at least 354 days. One injection of the vaccine, which has been precipitated by alum, produces a high degree of immunity which is not appreciably increased by 2 injections at a 9-days interval of smaller doses of the alum-precipitated vaccine.

Finlayson, M. H., and Grobler, G. M. (1941) *S. Afr. med. J.*, **15**, 125.

UNDULANT FEVER

(*Melitensis* and *Suis* Types)

See also B.E.M.P., Vol. XII, p. 361; and Surveys and Abstracts 1939, p. 584; 1940, p. 573.

Clinical Picture or Treatment

O. E. Hagebusch and C. F. Frei review the incidence and symptoms of undulant fever in children. A review of reported work shows a wide incidence of the disease, although the symptoms are often unnoticeable and spontaneous recovery is common. Tests were made on 182 infected children with indefinite symptoms. Blood culture tests were mainly sterile and of no value. The skin test is the most important, but should not be the sole test. A bacterial antigen was used and observations made 72 hours later to allow initial erythema to disappear. Opsonic and agglutination tests should follow. Diagnosis was based on a positive response to the three tests, the clinical picture and the exclusion of other aetiological possibilities. At the height of the fever, all tests may be negative and patients should be tested in intervening periods. The presence of *Brucella* in both mother and child is very frequent. Transmission

can take place through the placenta or the birth canal. Five cases of sterility in infected adult women are reported, but vaccination restored fertility.

Fever acquired by maternal infection is more severe and less self-limiting than that acquired by cow's milk. Seven patients were observed in whom inactive chronic brucellosis occurred during pregnancy. Three aborted, 2 continued normally after vaccination, and 2 had premature deliveries, stormy courses, and the babies had various disturbances including digestive upsets, rash, high fever, frequent colds, and diarrhoea. Serum is used for the treatment of acute disease and vaccine for chronic stages, but the serum has not yet been tried in infants. Oxidized *Brucella abortus* vaccine was used. Sixty per cent of those treated have discontinued without a return of symptoms, 20 per cent have improved but have had to continue treatment, and 20 per cent did not respond to any treatment.

Hagebusch, O. E., and Frei, C. F. (1941) *Amer. J. clin. Path.*, **11**, 497.

URAEMIA

See also B.E.M.P., Vol. XII, p. 379.

Treatment

Desoxycorticosterone acetate

H. Selye, experimenting with mice and rats, found that previous treatment with desoxycorticosterone acetate prolonged the survival time of animals in which acute uraemia had been produced by bilateral nephrectomy. Clinical trial will be necessary to show if this compound has a similar effect in uraemia due to kidney disease in the human subject.

Selye, H. (1940) *Canad. med. Ass. J.*, **43**, 333.

URETHRA DISEASES

See also B.E.M.P., Vol. XII, p. 386; and Surveys and Abstracts 1939, pp. 156 and 584; 1940, p. 574.

In Male

Anomalies

Congenital hypertrophy of verumontanum.—F. Pilcher, Jun. and H. W. Price report a case of congenital hypertrophy of the verumontanum in a male child admitted to hospital, at the age of 20 days, in a state of severe emaciation and moribund. The abdomen was soft and scaphoid, and both kidneys were palpable and larger than normal. The child died on the day of admission. At necropsy both kidneys were full of thick purulent urine. The markedly enlarged and elongated verumontanum projected into the bladder, and completely, or almost completely, occluded the urethra.

Inflammations

Trichomonas vaginalis.—W. G. Liston and R. Lees record 20 cases in males of infestation of the genito-urinary tract by *Trichomonas vaginalis*, a subject that has otherwise attracted very little attention in Great Britain. Analysis of 400 consecutive cases (excluding syphilis) in patients attending the male venereal department of the Royal Infirmary, Edinburgh, showed that 16, or 4 per cent, were due to this infestation, in 1 case combined with gonorrhoea. Among the 20 cases the site of infestation was the subpreputial sac in 5 cases, the anterior urethra in 9, the posterior urethra in 3, and extension to the bladder, seminal vesicles, or prostate in 3, in the last group the symptoms and signs being more severe. Approximately 10 per cent of the Edinburgh Venereal Diseases Department's cases of non-gonococcal urethritis in males were due to *Trichomonas vaginalis* infestation. The most satisfactory method of diagnosis is microscopical examination of suitably prepared and stained films, as introduced by W. G. Liston and W. A. Liston. The infestation, which is generally acquired from women with trichomonas infestation, is usually accompanied by trivial symptoms, and may pass unnoticed. The incubation period may be as short as one day, but often extends to 14 days. Extension to the prostate usually occurs late and cure is difficult. Treatment by irrigation or instillation of the urethra by antiseptics is not curative and often does harm. A strongly alkaline urine inhibits the development of trichomonas, relieves symptoms, and may produce clinical and permanent cure. Relapses are common. In a further paper, on the infestation in both sexes, W. G. Liston again refers to infestation of the male genito-urinary tract, and mentions that the parasite does not find a very suitable habitat in the male urethra and soon disappears. But persistent infestation may be due to repeated reinfection as in the case of a husband of a wife the subject of the disease. In these circumstances the parasite may, by amoebic movement, penetrate into the tissues and become established in and under the mucosa rather than be found on the surface of the mucous membrane. The detection of the trichomonas may be very difficult, and the fact that these later lesions are due to *Trichomonas vaginalis* must often be inferred from the previous history that the parasite had been recognized in the early stages of the disease when it still lived upon the surface of the mucous membrane.

Neoarsphenamine treatment.—W. H. Holbrock reports on the use of neoarsphenamine in non-specific anterior-posterior urethritis. The patient is treated for a few days by anterior-posterior instillations of 10 per cent solution of silver nucleinate and alkalis by mouth. As soon as acute symptoms have disappeared, generally in from 5 to 7 days, 6 to 8 ounces of 1 in 10,000 silver nitrate solution are instilled into the bladder. Red areas in the urethra are

touched with 4 per cent silver nitrate through an endoscope. The patient is then given intravenously 0.2 gramme of nearsphenamine in 10 cubic centimetres of distilled water. He is given $1\frac{1}{2}$ grains of ammonium nitrate, 4 times a day by mouth, to acidify the urine, and a silver irrigation every other day. Every 5 to 7 days the endoscope is passed, and 0.3 gramme of nearsphenamine is given. The treatment generally lasts for 3 weeks.

In Female

Congenital stricture

A. W. Adams reports a case of congenital stricture of the female urethra, in a woman, aged 35 years, who was thought to be pregnant. On catheterization under an anaesthetic 2 pints of urine were drawn off. There was a history of incontinence when a child, and of difficulty in micturition since then. Repeated straining and pressure were necessary to empty the bladder. The patient had a cystocele. The bladder was finally opened, and showed a ledge projecting forward at the region of the internal meatus; this was excised. After operation the patient was able to void urine easily and at a normal rate.

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— and Lees, R. (1940) *Brit. J. vener. Dis.*, **16**, 113.

— and Liston, W. A. (1939) *J. Obstet. Gynec.*, **46**, 474.

Pilcher, F., Jun., and Price, H. W. (1940) *J. Amer. med. Ass.*, **115**, 2072.

URINE EXAMINATION

See also B.E.M.P., Vol. XII, p. 393; and Surveys and Abstracts 1939, p. 585; 1940, p. 575.

Pyuria

Congenital obstruction and urinary infection

Children.—A. B. Hawthorne reports 85 cases of urinary infection in children (girls 61, boys 24), 45 being acute and 40 chronic. In 23 cases an acute infection elsewhere in the body preceded or accompanied the urinary infection, 17 being respiratory, and only 4 gastrointestinal, a much lower incidence than would ordinarily be expected. In a group of 16 girls with chronic urinary infection there were 4 with various other foci of infection, after removal of which the urinary infection was cured; in the remaining 12 cases there was some form of congenital obstructive anomaly usually in the upper part of the urinary tract, namely, uretero-vesical stricture, uretero-pelvic obstruction, renal hypoplasia, neuro-muscular dilatation of the ureter and pelvis, lack of rotation of the renal pelvis. Among 16 boys 12 showed congenital obstructive anomalies. Among the older boys there were 3 with an obstruction at the neck of the bladder, and the pathological picture so common in the older prostatic patient. Altogether 60 per cent of these chronic infections persisted because there was urinary stasis or obstruction due to some congenital abnormality in the urinary tract.

Hawthorne, A. B. (1941) *Canad. med. Ass. J.*, **44**, 152.

UROGENITAL ORGANS, ABNORMALITIES

See also B.E.M.P., Vol. XII, p. 401; and Surveys and Abstracts 1939, p. 586; 1940, p. 576.

Urethra

Congenital obstruction

Danger of infection.—H. F. Helmholz and G. J. Thompson emphasize the importance of early recognition and complete removal of any obstruction in the urinary tract before irreparable harm is done to the kidneys. It is pointed out that 5 per cent of infants have some congenital abnormality in the urinary tract. Infection is prone to be superimposed on urinary obstruction; now that urinary antiseptics, such as mandelic acid, sulphanilamide and sulphathiazole are available, the infection can be cured, but this does not prove the absence of urinary obstruction. Clinical recognition of congenital obstruction in the posterior urethra and at the neck of the urinary bladder, is not always easy, especially for an unskilled cystoscopist. It is of paramount importance that an infection should be treated after the obstruction has been removed, for in the absence of this post-operative treatment the bladder, ureters, and kidneys may undergo further unnecessary injury. A periodical examination should be made of the urine.

Kidneys, Ureters, and Bladder

Ureters

Surgical injuries.—A. H. Peacock states that many surgical injuries to the ureters occur. The possibility of accidental ligation of the ureter should be remembered in all pelvic surgical procedures. Any suspicion of ureteral injury should be investigated early by retrograde catheterization of the ureter or excretory urograms. The commonest injury, 63 per cent of all injuries, is unilateral ligation. Incision or severing of the ureter accounts for 25 per cent of injuries. Of these accidents, 63 per cent are associated with inter-ligamentous cysts, cancer, and large fibroids. The most satisfactory treatment is nephrostomy and, if necessary, nephrectomy later. The mortality is 25 per cent.

Helmholz, H. F., and Thompson, G. J. (1941) *Proc. Mayo Clin.*, **16**, 6.

Peacock, A. H. (1941) *Northw. Med.*, **40**, 132.

UTERUS, DISEASES AND DISORDERS: TUMOURS

See also B.E.M.P., Vol. XII, p. 448; and Surveys and Abstracts 1939, p. 588; 1940, p. 577.

Carcinoma*Carcinoma of cervix uteri*

Treatment by local refrigeration.—C. A. Gordon and J. V. Cresci report on the local refrigeration in 10 advanced cases of cancer of the genitals, 9 being carcinoma of the cervix and 1 of the vulva. In 6 cases the duration of therapy was 96 to 900 hours. The temperature was maintained between 40° F. and 50° F. in 1 case, at 50° F. in 3 cases, at 50° F. to 55° F. in 2 cases, and 60° F. in 1 case. A notable diminution in size of the tumour mass was observed in 3 cases, and pain was relieved in 2 cases. Serial biopsies showed cellular degeneration in only 1 case. Marked necrosis of the cancerous refrigerated area was found at necropsy in 3 cases.

Radium and X-ray therapy.—H. E. Schmitz and J. F. Sheehan describe the 5-year results from the treatment of cervical carcinoma with radium and super-voltage X-ray therapy with intensities of 500 kilovolts and over. Reactions in the skin, blood, and mucous membranes following treatment proved to be transitory, and no permanent changes were noted. A 5-year survival rate of 46.1 per cent was obtained which was a distinct advance over previous forms of treatment.

X-ray therapy.—R. Rosh analysed a large series of cases of carcinoma of the cervix treated by X-rays, and found that a good prognosis could be given in stages 1 and 2, if proper treatment is employed. In stage 3 the prognosis should be guarded as grading depends upon the experience and interpretation of the examiner. Some cases closer to stage 2 may give good results, while others closer to stage 4 or border-line cases, may not respond at all. If at all possible, treatment may be attempted even in clinically hopeless cases, with an occasional success. Success in all cases is governed by the general condition of the patient, the stage of the disease, the quality of irradiation used, the continuity of treatment, and the individual susceptibility.

Cobra venom for the relief of pain.—J. W. Kelso employed cobra venom for the relief of pain in carcinoma of the uterus and other conditions, with successful results. The dosage employed was $\frac{1}{2}$ cubic centimetre initially, and on succeeding days 1 cubic centimetre was given until relief was obtained or until 10 doses had been given. In many of the cases treated the relief of pain ranged from 85 to 100 per cent.

Associated endometriosis.—L. S. Kidd states that, in 10 per cent of cases of carcinoma of the cervix, there is an associated endometriosis of the lymphatic glands; these are of stony hardness and densely adherent to surrounding structures, but they react in a satisfactory manner to radiation. The disease must be diagnosed by careful inspection, early biopsy and the iodine test, when it is either in the almost stationary precancerous stage, or the small localized malignant plaque described by Schiller.

Haemangioma*X-ray therapy*

A. Y. Kevorkian reports a haemangioma of the uterus in a married woman aged 34. As it proved to be inoperable, a course of deep X-ray therapy was begun, consisting of 6 high-voltage treatments of about 400 roentgens each, 3 anteriorly and 3 posteriorly to the pelvis. There were 20-minute exposures over an area 30 × 30 centimetres, with 0.5 millimetre copper and 1 millimetre aluminium and a skin distance of 40 centimetres. Three similar courses were given within 15 months of the operative attempt with the result that the growth disappeared.

Fibromyomas*Radium and X-ray irradiation*

Irradiational treatment.—J. A. Corscaden reports that, in the treatment of 733 cases of uterine bleeding and fibromyoma of the uterus by radium and X-rays, the bleeding was controlled in 98.1 per cent of the cases. Of these 48 patients required supplementary irradiation. The failure of treatment in 14, or 1.9 per cent, of the cases was apparently due to one of the following factors; inadequate dosage; operation before sufficient time had elapsed for the irradiation to complete its effect; the condition being one of pedunculated submucous myoma; or unexplainable causes. Uterine tumour was satisfactorily reduced in 94 per cent of cases, if not larger than the size of a 3-months pregnancy, or in 40 per cent of cases, if larger. There were not any cases of carcinoma of the uterus discovered within two years after radio-therapy for benign bleeding or myoma.

Cysts*Primary hydatid cyst*

M. L. Welcker, G. D. Kaneb, and R. H. Goodale record a case of primary hydatid cyst of the uterus in a woman, aged 77, who was admitted to hospital with retention of urine and pain in the lower abdomen of three days' duration. In the lower part of the abdomen there was a large, firm, slightly tender, immovable tumour in the middle line. By pelvic examination a small polypoid mass was found protruding from the vaginal orifice. The uterus, which extended 75 centimetres above the symphysis pubis, was firm, suggestively fluctuant, and fixed; it was tentatively diagnosed as either an adenocarcinoma or a fibromyoma of the uterus with a protruding cervical polypus. Preparations for laparotomy were begun, but symptoms of cardiac failure rapidly proved fatal 9 days after admission to hospital. At necropsy the

uterus measured 14 centimetres in diameter, filled the pelvis, was symmetrically enlarged, and presented a smooth, pinkish-red surface. It contained a cyst 13 centimetres in diameter, with about 100 daughter cysts. There were not any cysts elsewhere in the body. Hydatid infestation of the uterus is usually secondary and due to leakage of an intra-peritoneal cyst, especially of the liver. The author has collected 42 previously recorded cases of primary hydatid disease of the uterus; this case appears to be the first published in North America.

Corscaden, J. A. (1941) *Amer. J. Roentgenol.*, **45**, 661.

Gordon, C. A., and Cresci, J. V. (1941) *Amer. J. Obstet. Gynec.*, **41**, 281.

Kelso, J. W. (1940) *Amer. J. Obstet. Gynec.*, **40**, 1050.

Kevorkian, A. Y. (1940) *New Engl. J. Med.*, **223**, 1.

Kidd, L. S. (1940) *Aust. N.Z. J. Surg.*, **10**, 123.

Rosh, R. (1940) *Radiology*, **35**, 17.

Schmitz, H. E., and Sheehan, J. F. (1941) *Amer. J. Roentgenol.*, **45**, 229.

Welcker, M. L., Kaneb, G. D., and Goodale, R. H. (1940) *New Engl. J. Med.*, **223**, 574.

UVEAL TRACT DISEASES

See also B.E.M.P., Vol. XII, p. 495; and Surveys and Abstracts 1939, p. 590; 1940, p. 579.

Inflammation

Special forms of irido-cyclitis

Uveo-parotitis.—S. I. Kaufman suggests that uveo-parotitis, in spite of its chronic and stormy course, has a tendency to recover spontaneously, and supports the contention by the case of a woman, aged 22, who was suddenly attacked by facial (Bell's) palsy on the right side, and a swelling in the left parotid area. Four days later both eyes became somewhat painful and reddened, and other characteristic signs and symptoms followed. The disease ran a chronic course for a year, being most intense during the first six months. During its height the media were so cloudy that no details of the fundi could be observed in spite of wide dilatation of the pupils. Gradually the media began to clear, the deposits on the cornea, iris, and anterior capsule of the lens began to disappear, and vision gradually improved. The treatment included the use of atropine sulphate, ethylmorphine hydrochloride, local heat, hyperthermic treatments, with a temperature of 105° F. maintained for 5 hours, and several courses of sulphanilamide.

Tuberculous.—E. R. Williams reports that a radiological study of the chest in 40 unselected cases of chronic irido-cyclitis showed that 24 had positive tuberculous findings in the lungs and, of these, 12 showed pulmonary and hilar changes resembling chronic miliary tuberculosis and sarcoidosis. These 12 cases were considered to be examples of chronic miliary tuberculosis of either haematogenous or lymphogenous origin, the latter cases showing changes due to lymphangitis reticularis chronica.

Tumours

Sarcoma

Prognosis.—T. R. Pahwa discusses the prognosis in sarcoma of the uveal tract, and states that three grades of malignancy can be distinguished from the histological types: Grade 1, spindle celled type A, a comparatively benign type in so far as, if other circumstances, such as early diagnosis and treatment, are favourable, there is hardly any death recorded from metastases in this group. Grade 2, spindle celled type B, more malignant than type A, but less so than other types. Grade 3, fascicular, epithelioid, and mixed cell types, very much more malignant than the other types, showing a mortality of about 40 per cent. Reticulin content appears to influence the prognosis considerably. From an examination of both the histological types and the reticulin content, it should be possible to estimate the prognosis in a very large number of cases.

Kaufman, S. I. (1941) *Arch. Ophthalm.*, N.Y., **25**, 659.

Pahwa, T. R. (1941) *Brit. J. Ophthalm.*, **25**, 241.

Williams, E. R. (1941) *Brit. J. Radiol.*, **14**, 116.

VEIN DISEASES

See also B.E.M.P., Vol. XII, p. 526; Cumulative Supplement, Key No. 1596; and Surveys and Abstracts 1939, p. 591; 1940, pp. 13, 137, and 580.

Obstruction

Clinical picture

Thrombosis of inferior vena cava.—J. A. Keen reports a case of complete obstruction of the inferior vena cava in a man aged 77. This was discovered accidentally in the dissecting room. There was nothing in the clinical history which gave any explanation of the cause of the venous thrombosis. The man had spent the last 11 years of his life in an infirmary, and had been ambulant. The inferior vena cava was entirely blocked by a mass of fibrous tissue containing an inner core of calcified material; this blockage extended from the level of the 5th lumbar vertebra to the groove in the liver, at which point the vessel is joined by the hepatic veins. The liver was of average size. This rare case demonstrates the remarkable potentialities of the body for establishing circulatory anastomoses, and makes it appear possible to establish a complete collateral circulation for the drainage of both kidneys.

Thrombosis of axillary and subclavian veins.—During the last 50 years 150 cases of thrombosis

of the axillary and subclavian veins have been reported, but according to J. R. Veal, who reports 17 more cases, the condition is commoner than this record indicates. The symptoms and signs are pain in the arm and shoulder; massive pitting oedema, weakness and partial loss of function of the arm; preservation of the radial pulse; elevation of systolic pressure on the affected side; cord-like swelling along the brachial basilic and axillary veins; elevation of local venous pressure; and lowered oxygen content of the venous blood of the affected arm. Veal suggests the following classification: (1) primary thrombosis, (a) thrombophlebitis (bacterial), (b) phlebothrombosis (non-bacterial), i.e. traumatic or effort thrombosis, or that due to over-distension of part of the axillary vein from violent respiratory effort with compression sufficient to cause obstruction at another point; (2) secondary thrombosis (a) due to regional infection, and (b) due to invasion of the vein wall or lumen by metastases from malignant disease of the axilla and chest; 60 cases following removal of the breast for carcinoma are collected; (3) the post-thrombotic syndrome, the author's title for the permanent results of venous obstruction. After the acute symptoms have abated there may remain sufficient obstruction in the vein to cause permanent elevation of the venous pressure in the affected arm. The amount to which the pressure is raised and the severity of the symptoms depend upon the extent to which a collateral circulation develops. If the collaterals are adequate there may not be any residual symptoms; they may be adequate to accommodate the venous flow during rest but not during exercise; or they may be inadequate even during rest, in which event the oedema is persistent. Veal considers that surgical measures, apart from multiple skin punctures to relieve the thrombosis, are not justified. Thrombophlebitis and phlebothrombosis are best treated by rest, elevation of the arm on soft pillows, and heat locally. Thrombosis secondary to malignant disease of the chest or axilla should be treated by rest and elevation of the arm.

Varicose Veins

Significance of small intracutaneous veins on the chest

H. Sahli in 1885 described the fine cutaneous phlebectasias running parallel to the lower anterior borders of the lungs and the attachment of the diaphragm in patients with chronic cough, and later recognized that they may be present in normal persons. They have often been ascribed to pulmonary lesions, such as chronic bronchitis and emphysema, pulmonary tuberculosis, pleuritic and pericardial adhesions, and cardiac failure. J. B. Burrett and D. Scherf examined 385 patients, in the main unselected, but including many instances of thoracic disease on account of the alleged relationship of pulmonary and cardiac disease to the veins. The patients included both sexes, ranged from 14 to 72 years, and a special effort was made to examine patients with diseases, such as peptic ulcer, diabetes insipidus, enteritis, unrelated to the circulatory system. Only intracutaneous veins, more or less dendritically arranged, and at the level of the pleural sinuses or around the last cervical and the 1st to the 5th dorsal vertebral spines were accepted. Of the 385 subjects, more than half, 261, were positive; phlebectasias were present in 28 only of 54 patients with pulmonary lesions (tuberculosis, emphysema, bronchitis); in 66, or 70.2 per cent, of 94 patients with failing heart. Among 137 subjects without demonstrable pulmonary or cardiac disease the veins were detected in 95, or 69 per cent. The incidence of the veins increases with age, may occur in normal persons and, as no morbid lesion in the chest is necessary, and as a congenital abnormality can be ruled out, some other explanation may be suggested; the authors mention that the tendency for bullae in emphysema to occur at the apices, the anterior margin of the lungs and bases, that is, at the same sites at which the pleural sinus veins appear, may be the result of a special elevation of pressure in these areas, during cough and pressure.

Treatment

Sensitivity to sodium morrhuate and monoethanolamine oleate (monolate).—R. F. Golden and W. W. Heyerdale report a case, in an unmarried housemaid aged 28, of hypersensitivity to sodium morrhuate and monoethanolamine oleate (monolate) when used by injection for varicose veins. The symptoms were severe, namely, convulsive twitchings, headache, vomiting, collapse, loss of consciousness, abdominal colic and diarrhoea, but of short duration. The monolate is theoretically free from protein, and the reactions following its use less frequent and not so severe as those caused by sodium morrhuate. Sodium morrhuate was first used at the Mayo Clinic for the injection treatment of varicose veins in 1930, and Alison Ritchie appears to have been in 1933 the first to describe varying degrees of toxicity and systemic reactions; she divided the reactions into (1) erythematous or urticarial skin manifestations; (2) gastro-intestinal disturbances, colic diarrhoea, soon after injection, and (3) collapse, pallor, low blood pressure, and temporary loss of consciousness. A few cases have proved fatal.

Wounds

Arteriovenous fistula

Diagnosis.—E. A. Nixon states that arteriovenous fistula causes a marked decrease in blood pressure and pulse rate, and that these factors, together with greatly increased capacity of the dilated vein, result in a compensatory increase in total blood volume and enlargement of the heart. Myocardial failure is not uncommon. Local symptoms of a side to side arteriovenous communication are thrill and bruit which are most intense during systole, and are directly over the site of the lesion. It is possible that cardiac failure may occur from over-

distension, so that venesection is important, if the diastolic pressure increases after closure of the fistula. Matas's aneurysmorrhaphy is desirable, but quadruple ligation is more often surgically practicable.

Treatment.—J. M. Waugh and H. B. Neel report a case of traumatic arteriovenous fistula of the femoral vessels in a man aged 42. The patient had received a bullet in the left thigh in 1918. There was profuse bleeding at the time of the injury, but not until 1 year later was a buzzing sensation detected in the thigh, and the foot became red when the limb hung down. There was cramp in the left calf at night. Symptoms became fairly severe, and the patient was operated on in 1923. In 1938 the patient struck the scar, an indolent ulcer formed, and the leg began to swell; the buzzing sensation returned. The aneurysm was dissected, and cure of the symptoms resulted.

Tumours

Primary leiomyosarcoma of the inferior vena cava

P. Hallock, C. J. Watson, and L. Berman record a very rare condition of which there was not an example among 34,000 necropsies in the pathological department of the University of Minnesota and only 4 published cases, those of Perl (1871), Unruh (1896), Melchior (1928), and König (1931). This was a primary malignant growth arising from the wall of the inferior vena cava and histologically a leiomyosarcoma in a woman aged 31. The previous cases were called myosarcoma, endothelioma, round-celled sarcoma. In the present case the tumour arose in the sub-diaphragmatic region of the inferior vena cava and extended into the right hepatic vein; it was adherent to the vein wall at one point and lying in the lumen obstructed the inferior vena cava. Clinically it resembled obliterating endophlebitis of the hepatic veins (Chiari's disease), but polycythaemia, a paradoxical pulse and, shortly before death a systolic blood pressure of 98 and a diastolic blood pressure of 90 millimetres of mercury were present. The differential diagnosis must be made from Chiari's disease, constrictive pericarditis, Pick's disease, and portal cirrhosis.

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Hallock, P., Watson, C. J., and Berman, L. (1940) *Arch. intern. Med.*, **66**, 50.

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Ritchie, Alison (1932-3) *Trans. Edinb. obstetr. Soc.*, 157.

Veal, J. R. (1940) *Amer. J. med. Sci.*, **200**, 27.

Waugh, J. M., and Neel, H. B. (1941) *Proc. Mayo Clin.*, **16**, 134.

VERTIGO

See also B.E.M.P., Vol. XII, p. 544; and Surveys and Abstracts 1939, p. 593; 1940, p. 583.

Labyrinthine or Aural Vertigo

Aural vertigo without suppurative

Ménière's syndrome treated with histamine.—B. T. Horton reports on the use of histamine, in the form of histamine acid phosphate or histamine diphosphate, in 49 cases of Ménière's syndrome. All the patients had vertigo, 33 had tinnitus, and 32 had some diminution of hearing. All the patients obtained prompt relief from vertigo, nausea, and vomiting, about 52 per cent were improved as regards tinnitus, and a small number reported improvement in hearing. Treatment is begun by giving 1 milligram of histamine base (2.75 milligrams of histamine diphosphate) in 250 cubic centimetres of physiological saline solution intravenously at the rate of 50 to 60 drops per minute by the gravity method. If the symptoms do not subside after the first injection, the injections can be repeated daily. A maintenance dose of 0.1 to 0.2 milligram of the drug can be given subcutaneously, 2 to 4 times a week. It is obvious that in Ménière's syndrome treatment should be predominantly medical.

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VITAMINS

See also B.E.M.P., Vol. XII, p. 570; Cumulative Supplement, Key Nos. 1601-1609; Surveys and Abstracts 1939, p. 594; 1940, pp. 16, 31, 56, 70, 114, 117 and 585; and pp. 5, 49 and 120 of this volume.

Water-soluble Vitamins

Vitamin B₁

In diabetes mellitus.—Some observations suggest the possibility that vitamin B₁ deficiency might be a factor in the development of diabetes mellitus and that treatment with thiamin might have a beneficial effect on this disease. Accordingly K. A. Smith and H. L. Mason made observations on three cases of well-established intensity of diabetes mellitus by variations in the amount of thiamin in the diet or given parenterally. It was found that there is not any evidence that the level of vitamin B₁ influences either the intensity of diabetes mellitus or the sensitivity of patients with diabetes mellitus to the action of insulin. M. G. Vorhaus had previously obtained negative results. The relatively mild degree of depression of tolerance for carbohydrates that has been found in intact animals and in men after long periods of deprivation of thiamin appears to represent a disturbance of metabolism not related to that involved in diabetes mellitus.

Hypovitaminosis B₁.—H. Pollack, M. Ellenberg, and H. Dolger state that the fermentation

test of A. S. Schultz, L. Atkins, and C. N. Frey for vitamin B₁ is clinically applicable because of its simplicity, inexpensiveness, and rapidity. The basis of the test is the stimulating effect of thiamin (vitamin B₁) on the rate of the fermentation of dextrose by yeast. The urine is tested by fermentation before and after parenteral injection of vitamin B₁, for the content of vitamin B₁. The test appears to be of value in the detection of the subclinical states of B₁ deficiency. The authors found that 25 per cent of 389 patients with various diseases, including anorexia, diarrhoea, effects of poor food, debilitating states, prolonged toxic states, and hepatic dysfunction, and all of four alcoholics tested were insufficiently supplied with vitamin B₁. Because of the known relation of vitamin B₁ to carbohydrate metabolism it has been inferred that diabetes mellitus might be due to vitamin B deficiency; 139 patients with diabetes mellitus were tested by this method, and did not lend support to this deduction. As the reliability of the test might be impaired by renal disorder, cases of renal insufficiency were excluded.

According to H. J. Borson, aneurin (vitamin B₁) is a non-threshold substance, and diuresis may wash out a considerable amount, thus contributing to the development of deficiency. He found moderate deficiencies of the vitamin in patients with thyrotoxicosis in spite of diets containing fair amounts of protective foods. In several patients with neuritis of uncertain cause, significant deficiencies were found. Fifty per cent of patients with disseminated sclerosis were markedly deficient, and 29 per cent showed definite symptomatic improvement after the oral administration of aneurin. Eighty per cent of patients with syphilis of the central nervous system were found to be deficient, and 58 per cent of these showed definite improvement after receiving aneurin.

R. D. Williams, H. L. Mason, R. M. Wilder, and B. F. Smith, in a study of 6 patients, found that a dietetic supply of 0.95 milligram of thiamin (aneurin hydrochloride) was not associated with any clear evidence of nutritional deficiency, but it provided less than a sufficient amount of this vitamin for the best nutritional state of the patient. It was found that a dietary restricted to 0.15 milligram of thiamin was tolerated for 147 days by 4 subjects during summer, whereas a similar dietary given to 4 other subjects during winter could be tolerated for 88 days only. Thus climatological factors may influence the rate at which evidence of thiamin deficiency appears. Similarly, physical activity influences the time taken for the onset of symptoms. It was found that the disease induced by restriction of the intake of thiamin differed from classical beri-beri in that oedema, cardiac dilatation, and peripheral pain were absent. The authors therefore felt doubtful if thiamin is the vitamin, lack of which is responsible for these classical features of beri-beri. The early stage of the disease induced by restriction of the intake of thiamin closely resembles neurasthenia, therefore states of thiamin deficiency in areas in which beri-beri and pellagra are rare, should be looked for chiefly in cases in which the diagnosis of neurasthenia has appropriately been made.

Hypovitaminosis and cardiovascular disturbances.—G. Konstam and H. M. Sinclair report about 3 patients, all living in Greater London, with cardiovascular disturbance, caused by deficiency of vitamin B₁. In 2 instances the diagnosis was confirmed by a very low amount of vitamin in the blood; in the third case a vitamin estimation was not made. The 3 patients, all males, were diagnosed respectively as 'beri-beri in a chronic alcoholic', 'beri-beri and scurvy with malnutrition and achlorhydria', and 'beri-beri and cirrhosis of the liver'. All 3 suffered from multiple neuritis and from achlorhydria or from hypochlorhydria, and responded convincingly to treatment by vitamin B₁, rest in bed on an adequate diet containing marmite, and without alcohol. There is little doubt that complete recovery from the cardiac and neuritic symptoms was due to the treatment by vitamin B₁. The clinical and other features of vitamin B₁ deficiency are reviewed. The usual cardiac symptoms are dyspnoea on exertion, palpitation, tachycardia, oedema, gallop or tic-tac rhythm of the heart, and 'pistol shots' heard over the peripheral vessels. Circulatory failure may be peripheral or central. As vitamin deficiencies are almost always multiple, controlled treatment is seldom justified, and any associated deficiency state, such as pellagra, scurvy, or anaemia, should be treated. W. G. A. Swan and F. Laws report a case in a man, aged 55, with a beri-beri heart, apparently due to a pure dietary deficiency of vitamin B₁. There was not any alcoholic excess, evidence of multiple neuritis, or pigmentation. A clinical cure followed the administration of vitamin B₁.

Vitamin B₂ complex

Choline as member of vitamin B₂ complex.—According to P. György and H. Goldblatt, experimental rations commonly employed in studies on the vitamin B₂ complex are generally low in content of choline. The addition of vitamin B₂ aggravates the specific effect of deficiency of choline, especially with regard to the development of cortical necrosis of the kidneys. Acute and subacute lesions are associated with this specific type of renal injury; the renal lesions and fatty infiltration of the liver, observed in rats kept on a vitamin B free diet supplemented with thiamin, riboflavin, and vitamin B₆, are indistinguishable from those attributed hitherto to cystine intoxication. The authors draw attention to the part played by choline as a potential member of the vitamin B₂ complex, and to the importance of the ratio cystine/methionine in the diet.

Vitamin B₆: pyridoxin.—J. Flexner and M. R. Chassin found that, after the intravenous injection of a test dose of pyridoxin, the urinary excretion of this vitamin in 12 of 14 patients under 50 years of age in one hour averaged 8.4 per cent of the amount injected. In 32 of 45

patients over 50 years of age it was 7.2 per cent, and in 13 it was 2.3 per cent. Six of 7 patients with post-encephalitic Parkinsonism showed a diminished output, averaging 2.5 per cent. Twelve of 14 patients with renal insufficiency, of varying degrees, showed a definitely impaired excretion of pyridoxin.

Therapeutic applications.—V. P. Sydenstricker states that the response of all grades of nicotinic acid deficiency to specific treatment with the vitamin (B_6) is rapid, and usually complete, although it is seldom possible to predict the dose necessary for cure or for maintenance. The normal requirement is probably about 25 milligrams a day. If the intake is increased to 300 or 500 milligrams, the cure of glossitis, stomatitis, and diarrhoea may be effected in about 2 days. Mild psychic disturbances disappear even more rapidly. Cutaneous lesions require from 7 to 14 days for complete resolution. In cases of severe pellagra, a dose of from 600 to 1,000 milligrams daily for 3 days is generally adequate for the relief of all urgent symptoms. After improvement has begun, the dosage may be reduced to 100–150 milligrams daily. The stuporous or encephalopathic patient may require 1,200 to 1,800 milligrams daily for 4 or 5 days.

Hypovitaminosis- B_6 .—P. Manson-Bahr states that glossitis, probably of a similar nature and non-specific to the disease, is present in pellagra, sprue, pernicious anaemia, the nutritional anaemias, and idiopathic steatorrhoea, and that, by reason of this and other features, such as changes in the spinal cord, these diseases are closely related to each other. He suggests, on the grounds of analogy as well as the results of treatment, that deficiency of the vitamin B_6 complex, which appears to be common to all, may partially explain these phenomena. He further suggests that nicotinic acid and riboflavin play an important part in the treatment of sprue as well as of pellagra, pernicious anaemia, subacute combined degeneration of the cord, and, to some extent, of idiopathic steatorrhoea. These diseases are so closely related to each other that borderline cases are seen to show the salient features of two or more of the group.

Xerostomia due to nicotinic acid deficiency.—W. Saphir obtained a striking curative effect with nicotinic acid in a case of xerostomia of long standing, thus suggesting the possibility of deficiency of nicotinic acid as an aetiological factor in the disease. The patient, a woman aged 49, had noticed for some years a progressively increasing dryness of the mouth which finally became so dry and painful that she had to take frequent sips of water. The mucous membrane of the entire oral cavity was completely parched and rough, and showed many cracks and fissures. After taking fairly large doses of yeast, thiamin chloride, and nicotinic acid for a fortnight there was considerable moisture present in the mouth, and the patient felt much relieved. When nicotinic acid was withheld, the condition rapidly became worse. Nicotinic acid alone in doses of 50 milligrams 3 times a day was capable of keeping the patient free of xerostomia.

Importance in human nutrition.—T. D. Spies, R. K. Ladisch, and W. B. Bean had previously (1939) described a syndrome characterized by extreme nervousness, insomnia, irritability, abdominal pain, weakness, and difficulty in walking which disappeared quickly after the intravenous administration of 50 milligrams of synthetic vitamin B_6 (pyridoxine). In 1940 they treated 20 similar cases in which there were residual symptoms of nutritional deficiency which could not be relieved by the use of synthetic nicotinic acid, synthetic thiamin hydrochloride, or synthetic riboflavin. Investigating the urinary excretion of injected pyridoxin in 5 normal males and 6 patients whose deficiency syndromes were showing clinical improvement, the authors found that after the intravenous injection of 50 milligrams of the substance, the average urinary excretion was 7.9 per cent in normal persons and 8.6 per cent in pellagrins who at the time did not have active vitamin deficiency. Nine ambulatory patients with clinical evidence of either pellagra, beri-beri, or riboflavin deficiency excreted an average of 0.5 per cent of the 50 milligrams of pyridoxin injected, with a range of 1.5 to nil per cent. The 4 patients in this group suspected of having a vitamin B_6 deficiency showed the lowest excretion of any studied, averaging only 0.2 per cent. The 3 patients with clinical deficiency disease who were admitted to hospital and put on a diet deficient in vitamin B_6 excreted hardly any of the injected pyridoxin. These results indicate that vitamin B_6 is important in human nutrition, and strongly support the hypothesis that clinical deficiency diseases occur, not as single entities, but as complexities.

Riboflavin deficiency and pantothenic acid.—T. D. Spies, S. R. Stanberg, R. J. Williams, T. H. Jukes, and S. H. Babcock report on the effect of pure pantothenic acid on human nutrition. They administered varying amounts of calcium or sodium pantothenate to 15 persons and observed that 100 milligrams of either salt may be injected intravenously without causing reaction and without significant change in blood pressure, pulse, temperature, or respiration. The blood pantothenic acid level of 28 patients with pellagra, beri-beri, and riboflavin deficiency was found to be decreased by 23 to 50 per cent, as compared with the levels of 18 normal persons. Injection of pantothenic acid was followed by a rise of from 20 to 30 per cent in the riboflavin level of the blood. The administration of 20 milligrams of calcium pantothenate daily, for 4 days, to 4 persons with cheilosis and typical ocular manifestations diagnostic of riboflavin deficiency caused similar temporary increases in the blood pantothenic acid and riboflavin. These values, however, returned to their previous levels when therapy was discontinued. The injection of 200 micrograms of riboflavin per kilo of body weight caused an increase of 80 per cent in the blood flavin concentration and of 45 per

cent in the pantothenic acid level. These observations indicate that pantothenic acid is essential to human nutrition, and that its function is probably associated with that of riboflavin.

Vitamin C

Effect on muscle response to histamine.—H. J. Friedman found that absence of vitamin C from the diet of guinea-pigs diminished the responsiveness of the smooth muscle to stimulation with histamine. In the muscles of animals with scurvy the minimal stimulating dose of histamine was at least 1,000 times as great as that needed for muscle preparations obtained from normal guinea-pigs. The change in the response of smooth muscles became apparent on the fourth day of a scorbutic diet. After this time there was little or no further change in the response of the smooth muscle to stimulation with histamine.

Role of vitamin C in wound healing.—A. H. Hunt finds experimentally that partial deficiency of vitamin C produces a most profound disturbance in the healing of clean wounds in guinea-pigs. Collagen does not form in the wounds, the intercellular substance remains immature and of poor holding power, and the proliferating mesodermal cells also fail to mature. If scurvy supervenes, the collagen of normally healed wounds reverts to pre-collagen. In a series of 28 human cases of wounds studied post-mortem, it was found that those most deficient in vitamin C showed the poorest collagen production. In 5 the failure to form scar tissue was a contributory cause of death, by facilitating the breakdown of the abdominal wound, leakage from the suture line, or both. The author concludes that vitamin C, in good concentration, is of the greatest importance in the healing of wounds. Even in a grossly deficient person, 1,000 milligrams of ascorbic acid daily, for 3 days, is enough to produce saturation. The daily dose should be divided so as to minimize the rapid excretion due to low renal threshold.

Vitamin C level in schoolboys.—L. J. Harris investigated the vitamin C level of 35 boys at an elementary school, by Harris and Abbasy's simplified saturation test. He found that 14 were below standard, and of these 5 were classified as showing a relatively severe deficiency. At a home for waifs and strays, on the other hand, where the diet was exceptionally good and included an orange each day, none of the 29 boys examined was below standard. The findings for the poor-class children agree with the results of dietary surveys such as those of J. B. Orr (1936) which have shown that the intake of vitamin C in working-class communities is often below the optimum. Intermediate results were found with boys having an intermediate diet.

Scurvy in the aged.—H. A. Rafsky and B. Newman draw attention to the contrast between the numerous researches undertaken into the clinical significance of vitamin C deficiency in early life on the one hand and the scanty interest taken in this subject in old age on the other hand. This neglect of gerontics is, and perhaps not unnaturally, a feature of medicine generally. The authors refer to two papers only on vitamin C in the aged, by J. Gander and W. Niederberger (1936) and L. L. Kirchmann (1939). Rafsky and Newman investigated the retention and excretion of ascorbic acid in 25 (males 14, females 11) 'normal' subjects between the ages of 66 and 83 years, living in a home and free from any active disease. Only 1 subject, who had long been an exclusive vegetarian, was found by Kirchmann to have the so-called normal cevitic (ascorbic) acid level of 1 milligram per 100 cubic centimetres. In the 25 subjects the amount of ascorbic acid in the blood 1 hour after the midday meal and in the urine at the end of 24 hours was estimated and these readings regarded as controls. Then varying amounts of ascorbic acid were given. When the dosage was comparatively high, ascorbic acid retention was usually noted and blood levels were also appreciably high; the retention curves are grouped as follows: (1) a more or less steady level of retained vitamin C occurred in 2 subjects, the saturation point being reached with relatively smaller doses than in the remaining 23 subjects, (2) in 7 subjects the saturation point was not reached, these subjects requiring progressively larger doses of vitamin C, and (3) the retention level after reaching the peak shows a variable drop from a slight to a sharp descent. The authors are investigating the relation of ascorbic acid retention to the more or less constant association of old age with arteriosclerosis, but are not yet able to report.

Nutrition in diabetes.—L. B. Owens, J. Wright, and Edna Brown studied the vitamin C nutrition in 100 diabetic patients who had been under treatment, and 25 untreated patients with diabetes mellitus. Two-thirds of these patients had a blood ascorbic acid level less than 0.80 milligram per 100 cubic centimetres. Of 50 non-diabetic patients, 90 per cent had ascorbic acid levels below 0.80 milligram per 100 cubic centimetres. Low-calorie diets, insulin administration, hyperglycaemia, and glycosuria had no apparent relation to the blood ascorbic acid content.

Vitamins C and P

Hypovitaminosis.—H. Scarborough, investigating deficiency of vitamins C and P in man, found that the administration of vitamin P did not control the large subcutaneous haemorrhages characteristic of the scorbutic state, whereas these haemorrhages were arrested within 24 hours by a large dose (500 milligrams) of ascorbic acid. The administration of vitamin P had no effect on other important manifestations of scurvy, such as tissue hydration, anaemia, knee flexion, and the general clinical condition. On the other hand, the administration of vitamin P can produce an increased capillary resistance in the scorbutic subject before or after treatment with ascorbic acid. The capillary resistance of such subjects is not controlled by the administration of ascorbic acid or of vitamins A, B₁, or D. A deficiency of vitamin P may exist in man, even when he has been taking large doses of ascorbic acid for long periods.

Its clinical manifestations include pains in the legs on exertion, pain across the shoulders, weakness, lassitude, and fatigue. It is always associated with a much decreased capillary resistance, and may be characterized by the development of spontaneous petechial haemorrhages, especially in areas exposed to pressure. There is no accompanying haematological abnormality. It responds to treatment with vitamin P.

Vitamin P

Effect on capillary fragility and permeability.—H. G. Rapaport and Sylvia Klein studied the capillary fragility in a group of 100 allergic children by means of a positive pressure test; of these 49 per cent showed abnormal capillary fragility. In a further investigation 12 children with repeated abnormal capillary fragility tests were given vitamin P, and followed periodically for at least 6 months. In all the capillary fragility tests became normal after the administration of vitamin P. The vitamin apparently plays an important part in the mechanism of permeability of the capillary wall, probably acting as an essential constituent for normal capillary permeability.

Fat-Soluble Vitamins

Vitamin A

Quantitative requirements.—P. R. McDonald states that the average daily requirement of vitamin A, in the case of adults, is 2,000 to 3,000 international units, and that a diet containing 500 cubic centimetres of milk, 1 egg, 25 grammes of butter, and 1 portion of vegetables is sufficient to meet these requirements. During pregnancy or illness at least 5,000 units are necessary. In a growing child 6,000 to 8,000 units should be sufficient. Patients with diseases of the liver, especially cirrhosis, are often found to be deficient in vitamin A and may require as much as 100,000 units a day.

Miners' requirements.—C. E. Kellett reports the results of an investigation of the vitamin A content of the diet of 40 Durham miners working underground, the majority for more than 20 years, with an average age of 42 years, which is practically that (42.3) said to show the maximum incidence of nystagmus or other defect of vision. It was found that the diet of some miners differs from that of the general population in that the vitamin A intake is high, the largest single source of vitamin A being butter, and the next liver. The addition of further quantities of vitamin A to these miners' diet did not cause any discomfort nor any material improvement in their power of dark adaptation. It is suggested that the diet should be maintained at the relatively high daily intake of 6,000 to 7,000 units of vitamin A.

Preferential solubility in mineral oil.—The use of mineral oil as a laxative or as a substitute for absorbable fat in reduction diets is known to be apt to produce deficiency of vitamin A, because carotene in the diet is absorbed by the oil and not utilized. Amounts as small as 15 or 30 cubic centimetres of mineral oil can remove all the carotene from a normal diet. A. C. Curtis and P. B. Horton attempted to overcome this difficulty by saturation of the mineral oil with carotene before administration; but as 100 cubic centimetres of oil can absorb nearly half a million units of vitamin A at body temperature, this is impracticable. As it is known, from reports of other workers, that vitamin A and carotene behave differently as regards preferential solubility in mineral oil, the authors tested the availability of vitamin A given in conjunction with mineral oil, by growth experiments on rats. Their results show that vitamin A given with mineral oil was as effective in promoting growth as vitamin A given in cotton-seed oil. They therefore recommend that when mineral oil is used as a cathartic, vitamin A should be combined with it, either by taking in addition fish-liver extract oil or by mixing the vitamin A with the mineral oil.

Vitamin D

Distribution after large doses.—H. Vollmer examined post-mortem a child, 3 years old, dead of lymphocytic leukaemia, who had received 2,260,000 units of crystalline vitamin D shortly before her death. There was no evidence of any damage due to hyper-vitaminosis. The brain did not show any evidence of vitamin D in the thalamus, hypothalamus, hippocampus, corpus striatum, frontal lobe, medulla, or pituitary. Three other children who had also received very large doses of vitamin D showed similar negative findings.

Vitamin E

In neuro-muscular disorders.—C. H. Shelden, H. R. Butt, and H. W. Woltman, in an endeavour to verify the various claims made about the value of vitamin E in some neuro-muscular disorders, gave wheat-germ oil by mouth, in doses of 45 cubic centimetres with each meal, supplemented by synthetic α -tocopherol in sterile peanut oil, in doses of 100 milligrams twice weekly to 18 patients. Eight of these had progressive muscular dystrophy, 6 had amyotrophic lateral sclerosis, and 4 had progressive muscular atrophy. Treatment lasted for from 3 to 5 months. The authors did not observe improvement in any case, but add that the negative results should not be interpreted as failure of these therapeutic agents in the treatment of these diseases. Possibly the duration of treatment was not long enough, or perhaps vitamin E is not effective in the absence of other vitamins or essential nutrient materials present in excess.

Treatment of muscular dystrophies and myotonias.—S. Stone states that vitamin E is important for normal muscle growth in infancy and childhood, and points out the probability that some forms of muscular dystrophy, some myotonias, and some cases of poor muscular development in infancy are expressions of vitamin E deficiency. The author finds that the administration of vitamin E is clearly of therapeutic value in such cases.

Vitamin K

Effect on prothrombin level.—J. W. Norcross and M. D. McFarland employed 2-methyl-1:4-naphthoquinone (synthetic vitamin K) intravenously in 22 patients. The minimal effective daily dose in the adult was found to be 2 milligrams, and this dose, in cases uncomplicated by hepatic impairment, raised the prothrombin level from 50 to 80 per cent in an average of $7\frac{1}{2}$ hours and to 100 per cent in an average of 20 hours; it maintained the level above 90 per cent of normal for 4 or more days unless liver damage was present; in patients with severe hepatic damage there was only a slight response to the drug, but otherwise bleeding was rapidly and effectively controlled.

F. S. Bruchsaler found that, in 30 normal infants, the average prothrombin time on the first day of life was 58.3 per cent, falling to 55.4 per cent on the fourth day, and then increasing to 57.1 per cent of the normal adult blood by the sixth day. The prothrombin level of another group of 30 normal new-born infants, to whom vitamin K concentrate was given for the first 6 days of life, rose from an average of 59 per cent to 70.9 per cent by the second day, to 80.9 per cent by the fourth day, and to 84.4 per cent of the adult normal by the sixth day. After the administration of vitamin K to 10 mothers while in labour, and during the first 6 days after delivery, the prothrombin level rose from 63.3 per cent on the first day to 75.3 per cent on the second day, to 83 per cent of adult normal on the fourth day, and remained at this level for the following 2 days.

Effect on prothrombin time in new-born infants.—R. B. Lawson finds that 1 milligram of 2-methyl-1:4-naphthoquinone (synthetic vitamin K) given intramuscularly to the new-born infant prevents hypoprothrombinaemia. From 2 to 4 milligrams of the drug given to mothers 6 to 12 hours before delivery prevents serious rises in the micro-prothrombin times of new-born infants. The routine administration of substances with vitamin K activity to expectant mothers or to new-born infants is advocated.

H. G. Poncher and K. Kato successfully treated 22 infants with hypoprothrombinaemia haemorrhagica neonatorum (haemorrhagic disease of the new-born) with synthetic vitamin K. The preparations employed were 2-methyl-1:4-naphthoquinone (vitamin K₃); 2-methyl-4-amino-naphthol hydrochloride (vitamin K₆), and an aqueous solution of 2-methyl-1:4-naphthoquinone with sodium bisulphite. These drugs were administered orally, intramuscularly, and subcutaneously in the order named. In most cases the effect of treatment was shown by shortening of the prothrombin time within 2 to 6 hours after medication. Clinical improvement was both prompt and permanent with all the preparations tested. Vitamin K is specific in the treatment of this condition.

I. N. Kugelmass states that human prothrombin prepared from plasma is a pseudo-globulin combined with alkaline salts, soluble in alkalis, sparingly soluble in water, stable at room temperature, iso-electric at a hydrogen ion concentration of 5.2, and with a clotting potency of 1:100,000. Infants' blood is undersaturated in prothrombin until the blood-volume reaches about one litre, and may therefore be increased in concentration by vitamin K administration. Children's blood, on the other hand, is saturated with prothrombin at the adult level, and is not influenced by the administration of vitamin K, so that a dietary adequate in milk and leafy vegetables provides ample amounts of this anti-haemorrhagic factor. Prothrombin deficiency in the blood-clotting mechanism is not a determining factor in haemorrhagic diseases of infancy and childhood, except in the relatively rare, latent or manifest haemorrhagic diseases of the new-born, pseudo-haemophilia hepatica, icterus gravis neonatorum, and occasionally in hereditary pseudo-haemophilia.

W. W. Waddell and G. McL. Lawson consider that hypoprothrombinaemia and associated haemorrhage are not likely to occur in any new-born infant treated with vitamin K through its mother, and supplemented during the first few days of life. The immediate cause of the bleeding is prothrombin deficiency, which is very frequent during the first few days of life, and prothrombin deficiency is in turn the result of hypovitaminosis K. There are indications that prothrombin deficiency may be a factor in many of the cerebral accidents of the new-born, especially in those cases in which the signs of intracranial haemorrhage are late in appearing, indicating that the haemorrhage is of a slow oozing character. Although trauma is the precipitating factor, the extent of existing damage may well depend on the degree of prothrombin deficiency. At present every infant born in the University of Virginia hospital is treated with vitamin K through the mother, and this treatment is supplemented by oral administration of the vitamin during the first few days of life. The authors' experience is that hypoprothrombinaemia and associated neonatal haemorrhage will not occur in infants thus treated, and that so-called traumatic birth-injury has been, and will continue to be, materially lessened.

S. Kove and H. Siegel found low prothrombin levels in 52 of 76 infants during the first 8 days of life. Wide variations in prothrombin levels occur in each of the first 8 days, but most commonly in the first 2 days. The average prothrombin level is at its lowest in the first 2 days, and then rises slowly, though it remains below the normal adult value. The dietary history in 68 of the 76 cases did not show any correlation between the maternal dietary vitamin K intake and the prothrombin concentration of the offspring. Vitamin K concentrations should be given prophylactically to the mother before labour, in order to assure high prothrombin levels in the new-born infant.

According to P. S. Astrowe, E. S. Palmerton, and Virginia Henderson, a haemorrhagic

tendency exists in the new-born infant between the second and fifth days of life, as evidenced by a raised prothrombin clotting time. As little as 2 cubic centimetres of vitamin K in the first 24 hours inhibits the upward swing in the prothrombin clotting time. A normal clotting time in the mother does not preclude a haemorrhagic tendency in her infant.

G. P. Bohlender, W. M. Rosenbaum, and E. C. Sage found that 4-amino-2-methyl-1-naphthol hydrochloride (synthetic vitamin K) given intravenously to the mother before delivery effectively prevents prothrombin deficiency in the new-born infant. The vitamin preparation has not any gross toxic effects on the baby during the first week of life. There is evidence that vitamin K readily passes through the placenta. The vitamin preparation should always be given when the infant is likely to be premature, if labour is prolonged, and if operative delivery of any type is anticipated.

A. E. Maumenee, L. M. Hellman, and L. B. Shettles find that infants with retinal haemorrhages show lower prothrombin levels than normal infants. The incidence of retinal haemorrhage in the new-born can be slightly reduced by the administration of vitamin K to mothers during labour. The prothrombin levels are not greatly raised in infants with retinal haemorrhage, born of mothers treated during labour. The administration of vitamin K to mothers before the onset of labour eliminates retinal haemorrhage in their infants almost entirely.

Prothrombin levels in labour.—J. E. Fitzgerald and A. Webster report their observations on the effect of vitamin K given to women in labour. Control patients showed practically no change in the maternal prothrombin during and after labour. Patients treated with vitamin K by mouth showed a distinct rise in the maternal prothrombin level at the end of labour. There was also a similar rise in the average level of the blood in the umbilical cord. Patients treated with synthetic vitamin K intravenously showed approximately the same rise of prothrombin levels. In a small number of patients given sodium pentobarbital as an analgesic, there was a definite fall in the prothrombin level of both mother and child. This depression can probably be prevented by the proper use of vitamin K.

Water-soluble and Fat-soluble

Vitamin B₆ and vitamin E

In amyotrophic lateral sclerosis and muscular dystrophy.—J. W. Ferrebee, W. O. Klingman, and A. M. Frantz gave vitamin E and vitamin B₆ preparations in large amounts to a group of patients with amyotrophic lateral sclerosis and with muscular dystrophy. Whilst under treatment, patients with amyotrophic lateral sclerosis became weaker, and had increased difficulty in walking, talking, and using their hands. Most of the patients with muscular dystrophy showed no change in their condition. The progress of the patients was followed for periods of 2 to 12 months.

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VULVA AND VAGINA DISEASES

See also B.E.M.P., Vol. XII, p. 606; and Surveys and Abstracts 1939, p. 600; 1940, pp. 22 and 592.

Vagina

Vaginitis

Trichomonas vaginalis.—W. Glen Liston reviews the present position with regard to infestation by the *Trichomonas vaginalis*, and describes his observations with coloured illustrations of the parasite. Among various points discussed are the morphology of the parasite, the differentiation of the species, the remarkable fact that it is confined to humans, and usually to the vagina, and has never been found free in nature. The presence of glycogen in the epithelial cells of the vagina appears to be necessary for the development of *Trichomonas vaginalis*, which has been thought to feed on the glycogen. The storage of glycogen in the vaginal epithelium has been connected with the presence of oestrogens in the body, derived in the baby from the mother's circulation, and therefore disappearing within 1 or 2 weeks; it reappears at puberty and persists until some years after the menopause. In females it is present during active sexual life, and is utilized by Döderlein's bacillus to keep the reaction of the vagina acid, but excess of this acid (pH 3.5 and 4) favours the growth of *Trichomonas vaginalis*. The symptoms of vaginal infestation are definite and may be acute, subacute, chronic, and latent. In acute cases the symptoms are irritation, dysuric frequency, with a discharge, creamy in consistence, and greyish-yellow in colour; the insertion of the vaginal speculum, which may be very painful, shows that the vaginal walls are diffusely red. The disease may be wrongly regarded as gonorrhoea. Typical chronic relapsing infestation is the most frequent form of infestation by trichomonas among pregnant women. The treatment must aim not only at destruction of the parasites, which can be done by a number of preparations, but must be directed to restoration of the glycogen in the vaginal epithelium and the establishment of Döderlein's bacillus. If the deficiency of glycogen is due to over-destruction of glycogen by trichomonas, the parasite may be removed by carbarson pessaries; if an endocrine dyscrasia is probable, oestrogens may be tried. If the circumstances which control the growth and development of Döderlein's bacillus are still more obscure, the use of vitamin B₁ has been suggested.

Treatment of trichomonas vaginitis.—A. H. Moore recommends the use of hexylresorcinol solution, or jelly, for the treatment of *Trichomonas vaginitis*. Uniformly good results were obtained in 87 per cent of the cases treated, and partial relief was obtained in 6.5 per cent. Following the use of the drug, itching and discharge subsided rapidly.

Treatment of post-menopausal vaginitis.—L. A. Gray and J. D. Gordinier employed diethylstilboestrol and diethylstilboestrol dipropionate in 111 cases of post-menopausal vaginitis, for an average of 3 months in each case. The dosage varied from 0.05 milligram to 5 milligrams of the dipropionate given parenterally daily or at intervals as long as 2 weeks. By mouth from 1 to 5 milligrams of diethylstilboestrol were given daily or at longer intervals. Of the patients with menopausal symptoms, 47 per cent showed great improvement, 24 moderate improvement, 2 per cent slight improvement, and 18 per cent no improvement. Of 97 patients with atrophic vaginal changes, 73 per cent were greatly improved, 20 per cent moderately improved, 4 per cent slightly improved, and 3 per cent not improved.

Treatment of senile vaginitis.—B. G. Wiesstien recommends the use of oestrogens in senile vaginitis. Relief was observed in 7 patients who received as little as 20,000 international units of oestrogenic substance, given parenterally. In 2 patients vaginal suppositories, each containing 2,500 rat units (12,500 international units) of oestrogenic substance were used. In 8 patients inunction alone was employed, 1 gramme (5,000 international units) of ointment being applied daily. One patient received only oral therapy (4,000 international units daily).

Primary diphtheritic infection.—J. Parks reports a case of diphtheritic vaginitis in a woman, aged 22, a rare condition in the adult. In this case the predominating vaginal infection was

primary diphtheria, with spontaneous expulsion of a complete cast of the vagina, followed by vaginal atresia.

Cysts and tumours

Hydrometrocolpos in infants.—P. J. Mahoney and J. W. Chamberlain report 4 cases of hydrometrocolpos in infancy. This consists of a cystic structure, the wall of which is an imperforate vagina together with the uterus, the canal of the latter being generally dilated, though only to a slight degree. The vagina is much dilated; its epithelium is flattened instead of ridged, and the fornices are obliterated so that, on gross examination, the junction of the vagina and cervix uteri cannot be distinguished, and this cystic structure contains a thin mucinous cloudy greyish or yellowish-grey fluid containing desquamated epithelial cells.

Vaginal fistulae

Operation for vesico-vaginal fistula.—A. B. Taylor describes a new operation for inoperable vesico-vaginal fistula, which gives excellent post-operative control of urine, and provides sphincteric action easily accommodated to the particular needs of the patient. The technique is as follows. An incision is made completely round the vagino-cutaneous junction. Flaps of vaginal lining membrane and skin are dissected up. The vaginal flaps are sewn from side to side in such a manner as to invert them. Similarly the skin flaps are sutured from side to side with an everting stitch. Before these sutures are tied, and if necessary before they are introduced, a stab wound is made through the anal sphincter just anterior to the anal margin; a long artery or sinus forceps is forced up through the anal sphincter and is cut down into the posterior vaginal wall at a point 1 to 1½ inches above the vaginal cutaneous junction. With the forceps a medium-sized catheter is pulled down through the track thus made. The catheter is cut off and anchored by a stitch, leaving from ¼ to ½ inch projecting on the vaginal and on the skin surfaces. The patient is then returned to bed. The catheter is allowed to remain in place for at least 6 weeks, this being the time considered necessary for completion of epithelization.

Vulva

Pruritus vulvae

Use of stilboesterol cream.—I. I. Lubowe reports on the use of stilboesterol cream in an aliphatic cholesterolized stearate base in the treatment of pruritus vulvae. Sixty grains of the cream are rubbed in morning and night; and in the evening, before retiring, an antiseptic douche is taken, followed by the introduction into the vagina of 60 grains of the preparation. The average time necessary to effect a cure in 12 cases was 2 to 3 weeks.

Elephantiasis of the clitoris

W. E. Coutts and O. Monetta describe a special form of elephantiasis affecting chiefly the prepuce of the clitoris, and to which they applied the term 'peniform hypertrophy of the praeputium clitoridis'. The syndrome is uncommon, having been found by the authors in 5 of 66 women with elephantiasis vulvae of a lymphogranulomatous nature. The initial stage is characterized by a varying degree of elephantiasis of the labia majora, glans, and prepuce of the clitoris, which appears like the knob of a bell lying between the infiltrated labia majora. In the more advanced stage the hypertrophied parts protrude between the labia and hang downward. Such a formation is covered on its outer surface by skin, and posteriorly by mucosa. In the final stages the structure hangs before the external genitalia like a penis and completely covers the urethral and vaginal orifices.

Leucoplakia vulvae

Mercury sulphide tattoo.—R. Turell successfully treated a patient with intractable pruritus due to leucoplakia-kraurosis by the intracutaneous deposit of mercury sulphide by tattoo, after a partial vulvectomy and four subsequent surgical procedures for the removal of involved or recurrent areas of skin had failed to control the pruritus. The perianal and perineal region were tattooed with the drug under infiltration anaesthesia with 1 per cent procaine hydrochloride. A week later the vulva was similarly treated. One month later the skin about the introitus and in the perianal region, with the exception of the perineal area, was normal in appearance.

Vulvar fusion

Dangers.—M. F. Campbell, discussing vulvar fusion, states that the chief considerations are the recognition of the anomaly in order to differentiate it from hermaphroditism and other unusual genital maldevelopments, and the establishment of free urinary drainage to prevent genital inflammation by the irritating action of retained decomposing urine. In most cases the removal of this irritation may be expected to prevent masturbation. Unless the labial fusion is dealt with in early childhood, it is liable to cause not only retention of menstrual flow, with its accompanying pathological alterations and dangers, but also to become more dense in later years and subsequently to prevent intercourse. The condition is one of the many unusual causes of pus in the voided specimen, so often diagnosed as pyelitis. The attempt to perform catheterization will readily disclose the anomaly, and catheterization will not be readily accomplished until the labial fusion has been corrected.

Tumours

Epithelioma of the vulva.—J. M. Waugh states that epithelioma of the vulva is best treated by radical vulvectomy, preceded about 2 weeks previously by bilateral dissection of the inguinal glands. If glandular involvement is present, post-operative deep X-ray therapy

over the groin and pelvis is of value. As kraurosis vulvae, if neglected, may become malignant, simple vulvectomy with excision of all the involved tissue is in order. The author has observed a low-grade adenocarcinoma in the small sebaceous cysts often present about the vulva, and advises the removal of such cysts, without rupture, even though they appear to be insignificant. In primary carcinoma of the vagina radium therapy is advisable; occasionally these lesions can be destroyed by fulguration, and this should be followed by irradiation.

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WHOOPIING-COUGH

See also B.E.M.P., Vol. XII, p. 616; Surveys and Abstracts 1939, p. 601; 1940, p. 594; and p. 68 of this volume.

Complications and Sequelae

Pneumonia

Sulphapyridine therapy.—J. L. Kohn, H. J. Rubin, and H. M. Hobart treated 33 children with pneumonia occurring during whooping-cough, with sulphapyridine in the usual dosage. Of these children, 60 per cent were under 2 years of age. In 12 a pneumococcus was isolated from the pharynx or larynx during the illness. The patients were grouped into the mild, moderately ill, and severely ill. There were 5 deaths. The group in which the pneumococci were found did no better than that in which other bacteria were found. Sulphapyridine had apparently very little effect on the course of the illness in those considered to be severely ill. Agranulocytosis was developed in 2 of the children as a result of the treatment, and 1 died. The authors consider that the drug should not be given for more than 6 days, and should not be repeated if there is an exacerbation of symptoms.

Susceptibility

Intracutaneous test

M. Weichsel, H. J. Rubin, P. Cohen, and J. H. Lapin describe a method of intracutaneous testing for susceptibility to whooping-cough. In 90 patients, 69, or 76.6 per cent, gave positive reactions during the course of the active disease. In a control group of 367 children with a negative history of whooping-cough, 70.8 per cent gave a negative, 10.6 per cent a doubtful, and 18.5 per cent a positive cutaneous reaction. Of 23 healthy children with a positive history of whooping-cough, 17 had positive cutaneous reactions, in some cases 7 years after having had the disease.

Treatment

Curative

Intranasal soluble antigen.—C. M. Burpee and W. A. Wilkes treated 22 active cases of whooping-cough by an antigen instilled into the nose daily. Forty per cent of the patients were greatly improved, 23 per cent were improved, and 37 per cent were not improved. There were not any reactions noted. The average number of paroxysms before treatment was 20 in the 24 hours, with an average duration of 1 minute. In cases responding to the antigen there was a notable decrease in the incidence, severity, and duration of the paroxysms in a few days, and by the end of 1 week the paroxysms had decreased to 4 or 5 very mild attacks, lasting only about 10 to 20 seconds, without any vomiting. The antigen contained the soluble protein of about 20 billion organisms. The drops were instilled into both nostrils, with the head hyperextended, and the child kept in this position for about 4 or 5 minutes.

S. H. Tabor, H. Weisler, and A. M. Litvak treated in hospital 38 cases of whooping-cough with whooping-cough vaccine. There appeared to be a small reduction in the number of paroxysmal coughs on days on which specific therapy was given. Limited therapeutic value was noted when the first 3 days of therapy were compared with the sixth, seventh, and eighth days. Local complications were not noted.

Curative and prophylactic

Antigen.—C. L. Joslin and T. A. Christensen report the results of the treatment of 1,051 cases with a whooping-cough antigen. The most suitable dose of antigen appeared to be 1.5 to 2 cubic centimetres. Four doses were given at intervals of 2 to 5 days. The antigen apparently assisted in the treatment of whooping-cough, when given early, by reducing the incidence of complications, and by shortening the duration of the attacks. The antigen also seemed to give a considerable degree of protection in the prophylaxis of whooping-cough, both before and after exposure to the disease.

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YELLOW FEVER

See also B.E.M.P., Vol. XII, p. 660; Cumulative Supplement, Key No. 1616; Surveys and Abstracts 1939, pp. 145 and 604; 1940, p. 596; and p. 99 of this volume.

Virus and Vectors

Cultivation of virus

New method.—G. M. Findlay and F. O. MacCallum describe a new method of cultivating the yellow fever virus *in vitro*, by employing an oxygenated culture medium. No change was noted in the pathogenicity of the virus for mice, and titration of the virus showed that it was pathogenic, on intracerebral injection into mice, in dilutions of 10^{-3} or 10^{-4} , an end-point equal, or superior, to that by culture in flasks.

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INDEX

A

- Abdominal
 - hyperaesthesia, cutaneous, in dyspeptics, 215
 - pain, spinal appendicitis, 125
- Abortion
 - habitual, 17
 - implantation of progesterone, 384
 - incomplete, conservative treatment of, 126
 - induced, tetanus following, 126
 - spontaneous and induced, relative incidence of, 17
 - threatened,
 - and habitual, pregnenolone therapy, 126
 - implantation of progesterone, 384
- Abortus fever
 - bacteriology, 126
 - laboratory infection in man, 126, 127
 - sulphonamides in, 126
- Abscess
 - cerebral,
 - fungous infection and, 173
 - in relation to congenital heart-disease, 174
 - otitis media complicated by, 217
 - epidural, of spine, 397
 - extra dural, suppuration of middle ear complicated by, 216
- Acacia
 - nephrotic oedema treated by, 314
- Acarines, 390
- Acarus Scabiei*. *See also* Scabies, 391
- Acetanilide poisoning, 409
- Acetarsone, syphilis treated by, 404
- Acetyl- β -methylcholine
 - asthma treated by, 333
 - parasympathetic tropism of, 333
- Acetyl- β -methylcholine bromide
 - megacolon treated with, 303
- Acetyl- β -methylcholine chloride
 - intravenous drip administration, 346
- Acetylcholine, effect on heart, 333
- Acetylglycarnobenzene, syphilis treated by, 404
- Achalasia
 - cardiac sphincter, of, supervision of squamous-celled carcinoma, 128
 - pharyngo-oesophageal sphincter, of, 128
- Acholuric jaundice. *See* Jaundice
- Acidosis, blood in, 128
- Acne vulgaris
 - cryotherapy, 129
 - psychological reactions, 128
- Acoustic neurofibroma, 174
- Acriflavine
 - components, bacteriostatic values of, 330
 - infected wounds treated by hypertonic sodium sulphate and, 268
 - prevention of nasal sepsis and post-operative scarlet-fever, in, 330
 - proflavine and, 330
- Acrocyanosis, cervico-thoracic sympathectomy for, 226
- Acromegaly, pain in hands and feet, 129
- Acropachy, 274
- Acrosclerosis, Raynaud's phenomenon associated with, 374
- Actinomycosis
 - abdominal, sulphonamide therapy, 129
 - treatment, sulphonamides, 118, 129
- Actinothorax, 129
- Adams-Stokes syndrome
 - electrocardiogram in, 246
 - heart-block and, 246
- Addison's disease, 131
 - cardiac failure after desoxycorticosterone, 132
 - clinical picture, 131
 - diagnosis, value of potassium tolerance curve, 131
 - treatment,
 - adrenal grafting, 132
 - implantation of desoxycorticosterone acetate pellets, 131
 - sublingual administration of desoxycorticosterone acetate, 131
- Adenitis, inguinal, lymphopathia venereum causing, 300
- Adenoids, operative technique, 130
- Adenoma, bronchial, 77
- Adiponecrosis e frigore, 226
- Adiposity, 130
 - children, in,
 - harmful effects of endocrine therapy, 130
 - treatment by benzedrine sulphate, 130
- Adrenal
 - cortex,
 - feminism in hyperfunction of, 133
 - hyperfunction of, 133
 - hyperplasia, 133
 - hypertrichosis in female caused by, 243
 - renal hypernephroma and virilism associated with, 133
 - neoplasm, 133
 - cortical extract,
 - bromide eruptions treated by, 213
 - pre-administration of, 387
 - treatment of shock due to burns, in, 181
 - glands,
 - atrophy of, and spontaneous hypoglycaemia, 260
 - diseases, 131
 - grafting, in Addison's disease, 132
 - haemorrhage,
 - acute bilateral, 132
 - fatal, in pregnancy, 358
 - meningococcal septicaemia associated with, 186
 - hypoplasia and insufficiency, 131
 - melano-carcinoma, with widespread metastases, 133
 - tumours, 133
 - metastases simulating aneurysms, 133
 - secretions, rôle in shock, 386
- Adrenalectomy, effects in rats, 132
- Adrenaline, procaine and, 112
- Aerocele, cervical, 311

INDEX

- Aero-otitis media, 182
- Age
estimation from teeth and jaws, 303
old. *See* Old age
peptic ulcer, relation to, 326
- Agglutination reactions, in glandular fever, 235
- Agranulocytosis
aetiology, 134
sulphapyridine causing, 134, 343, 344
sulphathiazole causing, 134
- Air
dust-borne organisms in, 185
hospitals, irradiation of, in, 130
- Air-borne infection, diphtheria, 209
- Air-raid casualties
blast injuries of lungs, 297
crush injuries, 269
psychiatric, 363
surgery of, 265
X-ray examination, 371
- Air-raids, civilian reactions to, 363
- Air-sickness, 36
- Albucid
burns treated with, 182
gonorrhoea treated by, 237
- Alcohol
estimation in urine, 134
injection, in migrainous neuralgia, 307
lavage, acute peritonitis treated by, 330
subarachnoid injections of, for pain in cancer, 185
toxic effects of, 134
- Alcoholic
beri-beri and vitamin B deficiency, 135
oesophagitis, 134
psychoses, 369
- Alcoholism, 134
acute,
effect on vision, 134
estimation of alcohol in urine, 134
cerebrospinal fluid pressure in, 188
chronic,
beri-beri and vitamin B deficiency, 135
cerebral changes, 134
oesophagitis in, 134
pellagra and, 324
gastritis caused by, 135
pre-cirrhotic hepatitis, 135
- Alimentary
diseases, 3
tract,
diseases, 24
infection in lymphopathia venereum, 300
- Alkaline powder, excessive use of, in gastric ulcer, 135
- Alkalis, use in induction of labour, 279
- Alkaloids, toxicology, 409
- Alkalosis, alkaline treatment causing, 135
- Allergens bacterial, sensitization to, in dermatitis herpetiformis, 204
- Allergic eczema
cataract and, 137
infants, of, 137
- Allergy, 135, 136
aetiology and pathology, 136
diagnosis, 136
food, 138
fungus infections causing, 137
gastro-intestinal, milk as cause of, 138
- Allergy—*continued*
histaminase skin tests, 136
histamine, rôle of, 136
milk as cause of, 138
skin, of, 137
fungous disease causing, 137
histaminase in treatment, 137
treatment,
histaminase, 137
potassium chloride, 136
- Altitude
effect on intracranial volume, 160
high, intra-ocular pressure at, 160
sickness, 32
- Aluminium hydroxide
colloidal, peptic ulcer treated by, 327
peptic ulcer treated by, 327
- Aluminium phosphate gel, peptic ulcer treated by, 327
- Amethocaine hydrochloride, 113
- Amino-acetic acid, effect on muscular fatigue, 331
- Amino-acids, in food, 232
- Aminophylline
peripheral blood flow, effect on, 331
treatment in,
angina pectoris, of, 144
bronchial spasm, of, 158
- Ammoniated mercury ointment, idiosyncrasy in children, 332
- Ammonium
chloride
control of bismuth therapy by, 404
convulsant therapy in mental disorders, 368
mandelate, 112
salts as expectorants, 178
- Amnioplastin, use in surgery, 264
- Amoebiasis cutis, 138
- Amyloid disease, 138
- Amyotrophic lateral sclerosis
vitamin B₁₂ therapy, 428
vitamin E therapy, 307, 428
- Anaemia, 139
aplastic, idiopathic, treatment by intra-sternal introduction of bone marrow, 141
- Baghdad spring, 140
- blood loss causing, 139
- Cooley's erythroblastic, 140
- erythroblastic, 140
- erythrophagocytic, 140
- haemolytic, 139, 140
acute or subacute, 140
chronic, with haemoglobinuria, 140
familial crisis, 139
Lederer's, 140
terminating carcinoma of stomach, 401
- haemolytica neonatorum, 140, 141
- hypochromic deficiency, 139
- idiopathic aplastic, treatment of, 141
- pernicious. *See* Pernicious anaemia
- post-haemorrhagic, 139
- secondary, caused by sulphanilamide, 344
treatment, concentrated suspension of red cells, 168
- Anaesthesia, 142
avertin, 142

INDEX

- Anaesthesia—continued**
 basal narcosis, 142
 hexobarbitone soluble (evipan sodium), 142
 children, pre-anaesthetic sedatives for, 143
 choice of anaesthetics in shock, 388
 intravenous, 143
 labour, in, 280
 local,
 herpes zoster treated by, 256
 muscular rheumatism treated by injection of, 229
 percarine, ocular sensitivity to, 338
 procaine hydrochloride, 142
 nitrogen monoxide and oxygen, 282
 opium as pre-anaesthetic sedative, 143
 perineal, in labour, 280
 pre-anaesthetic sedatives, 143
 rectal, 142
 spinal,
 maintenance of blood pressure during, 142
 neosynephrin for maintaining blood pressure, 142
 urinary retention after, 162
 Anal canal, carcinoma, squamous-celled, 147, 148
 Analgesia, in labour, 280
 Anastomosis, soluble rod method of vascular, 264
 Androgen
 effects on cancer tissue, 183
 rate of excretion of, 384
 Aneurin, administration in diabetes mellitus, 206
 Aneurysm
 aortic, 143
 abdominal, 143
 diagnosis, 143, 144
 syphilis causing, 143
 pulmonary stenosis and, 143
 carotid, internal, causing aural haemorrhage, 144
 coeliac artery, with symptoms of acute cholecystitis, 143
 dissecting, secondary to renal calcification, 144
 internal carotid, 144
 metastases from hypernephroma simulating, 133
 peripheral, 144
 pulmonary artery, 144
 splenic artery, of, 398
 Angina
 pectoris, 144
 pain, 144
 treatment, aminophylline, 144
 throat, associated with mononucleosis, 235
 Vincent's. *See* Vincent's angina
 Angiomatosis, retinae, treated by catholysis and surface diathermy, 377
 Angiotinin, rôle in hypertension, 165
 Angular depth perception apparatus, 31
 Anidrosis, 147
 Ankle
 fracture, osteoarthritis as complication of, 211
 tuberculous, treatment of, 274
 Ankylosing spondylitis, 155
 Anonychia, partial, with bony changes, 230
 Anorchidism, 231
 Anoxia, in aviators, 32
 Anthelmintic, phenothiazine as, 122
 Anthracite dust, effect on tubercle bacilli, 415
 Anthrax, treatment, serum and neokhar-sivan, 147
 Antibodies, in poliomyelitis, 356
 Antigen, whooping cough treated by, 431
 Antipyretic drugs, cancer treated by, 339
 Antiseptics, 10, 11
 barberry root, 332
 chlorophyll, 333
 sulphonamides, 114
 urinary, sulphonamides as, 117
 Antiseptic snuffs, 331
 Antiserum, pneumococcal meningitis treated by sulphonamides and, 304
 Anti-spasmodic, benzyl- β -dimethylamino- α -phenyl- α -ethylpropionate hydrochloride as, 333
 Antitoxin
 botulism treated by, 173
 diphtheria, 209, 260
 tetanus, 407
 Antuitrin-S skin test, in diagnosis of pregnancy, 357
 Anuria
 bismuth causing, 410
 potassium salts and, 408
 sulphapyridine calculi causing, 161
 sulphonamides causing, 346
 Anus
 carcinoma, squamous-celled, 147, 148
 diseases, 147
 faecal soiling of perianal skin, 147
 Anxiety states, convulsion therapy, 80
 Aorta
 abdominal, occlusion of, 153
 aneurysm. *See* Aneurysm, aortic
 right-sided, 246
 syphilitic lesions of, 249, 250
 Aortic
 arch, right-sided, 246
 valve,
 insufficiency, systolic pressure in extremities in, 252
 syphilitic endocarditis, in, 249
 Apnoea neonatorum, 156
 Appendicitis, 148
 acute,
 complications, 148, 149
 conditions simulating, 125
 mortality, 149
 old age, in, 148
 post-operative acute hepatitis, jaundice, and bleeding, 149
 prognosis, 149
 rheumatic fever associated with, 377
 treatment, ambulatory, 148
 chronic, clinical picture, 149
 oxyuris infestation and, 149
 spinal, 125
 Appendix
 epiploica, torsion of, 125
 oxyuris vermicularis in, 149
 Aqueous humour, concentration of sulphonamides in, 342
 Arrhythmia, 149

INDEX

- Arsenic**
 compounds,
 toxicity, 332
 trypanosomes, effect on, 332
 dermatitis, herpes simplex associated with,
 256
 effect of thiosulphate on excretion of, 404
 poisoning,
 cerebral symptoms, 410
 peripheral neuritis, vitamin B therapy,
 410
 Arsenical compounds, syphilis treated by,
 404
 Arsenoxide
 syphilis treated by, 105
 Arsphenamine
 dermatitis, 332
 encephalopathy caused by, 332
 harmful effects of, 332
 jaundice caused by, 332
 myocarditis, acute interstitial, caused by,
 332
 purpura haemorrhagica due to, 213
 Arterial circulation
 action of vasodilator drugs, 151
 method of increasing arterial flow to an
 extremity, 151
 plethysmographic method of measuring
 peripheral flow, 151
 Arteries
 ageing of, 151
 diseases, 150
 Arteriosclerosis
 infantile, 152
 intercapillary glomerulo-sclerosis and, 152
 Arteriovenous fistula
 diagnosis of, 421
 treatment, 422
 Arteritis
 chronic, 151
 temporal, 152
 Artery, splenic, aneurysm of, 398
 Arthritis, 153
 rheumatoid. *See* Rheumatoid arthritis
 Artificial respiration, indications for prone
 pressure method, 212
 Ascariasis, treatment by phenothiazine, 156
 Ascites
 foetal, obstructed labour due to, 279
 hepatic cirrhoses and, associated with
 hernia, 255
 Ascoli's treatment of splenomegaly, 398
 Ascorbic acid
 content of blood in asthma, 157
 diabetes mellitus treated by, 206
 gingivitis treated by, 308
 intravenous injections, in corneal condi-
 tions, 198
 Asphyxia
 children, in, 156
 new-born, in, 156
 causes, 156
 treatment, 156
 helium-oxygen mixture, 156
 oxygen, 156
 Asthenia, neurocirculatory, 2. *See* Effort syn-
 drome
 Asthma, 157
 aetiology, 157
 ascorbic acid, relation to, 157
 Asthma—*continued*
 bronchostenosis complicating, 157
 clinical picture, 157
 gum acacia causing, 157
 morbid anatomy, 158
 pulmonary eosinophilia and, 157
 relation to infections of upper respiratory
 tract, 157
 specific sensitisation 157
 status asthmaticus 158
 treatment, 158
 acetyl- β -methylcholine, 333
 aminophylline, 158
 choline derivatives, 333
 perisymphathetic injection, 158
 theophylline mono-ethanolamine, 158
 types in adults, 157
 vitamin C, increased demand for, 157
 Atebrin, in treatment of giardiasis, 24
 Atelectasis
 aetiology, 290
 massive, in new-born, 290
 Athetosis, double or bilateral, 159
 Athletic injuries, 159
 Atresia
 duodenal, congenital, 272
 oesophagus of, congenital, 318
 Atrophy, optic, tryparsamide therapy in, 162
 Atropine
 methylnitrate. *See* Eumydrin
 poisoning by, 409
 sulphate, retinitis pigmentosa treated by,
 376
 Audiometric tests, of aviators, 160
 Auditory acuity, effect of aircraft noise on, 36
 Aural
 haemorrhage, caused by aneurysm of in-
 ternal carotid, 144
 infections, sulphonamides in, 118
 vertigo, 422
 Auricular fibrillation, aetiology, 150
 Auscultation, of heart, 245
 Avertin
 anaesthesia, 142
 ureteral calculus treated with, 276
 Aviation, 159
 air-sickness, 36
 blackening-out, 33, 34
 cold, protection against, 35
 deafness, 160
 effect of altitude changes on intracranial
 volume, 160
 fatigue in, 35
 glare, protection against, 36
 hyperventilation in, 159
 intra-ocular pressure at high altitudes, 160
 maintenance of physiological efficiency of
 flying men, 32
 medicine. *See also* Flying
 medicine, 29
 cardiovascular stability, 30
 flying aptitude, 29
 high-altitude flying, 30
 psychological pre-selection of personnel,
 32
 stereoscopic vision, 31
 night-vision, 30, 31, 36
 noise, effect of, 36
 oxygen want, 32
 parachute descents, 33

INDEX

Aviation—*continued*

- visual problems, 36
- Aviators
 - aero-otitis media in, 182
 - audiometric tests of, 160
 - deafness in, 160
 - maintenance of physiological efficiency, 32
 - peptic ulcer in, 160
 - special senses, examination of, 160
 - vision of, 36
- Avoleum, 327. *See also* Vitamin A,
- Axillary veins, thrombosis of, 420, 421
- Azoman, 79. *See also* Cardiazol,

B

- β -erythroidine hydrochloride, encephalitis epidemica treated by, 332
- β -methylcholine urethane, in treatment of urinary retention, 161
- Babinski and crossed plantar responses, 376
- Babinski's sign, interpretation of, 376
- Bacillus*
 - proteus*, wounds infected by, 267, 268
 - tuberculosis*,
 - effect of anthracite dust on, 415
 - sulphapyridine, effect of, 415
 - unsuspected carriers of, 414
- Backache, 161
- Bacteria, spore-forming, in milk, 232
- Bacterial allergens, sensitization to, in dermatitis herpetiformis, 204
- Bacteriostatic values of acriflavine and proflavine, 330
- Bacterium*
 - enteriditis*, infection, complicating cerebro-spinal fever, 186
 - monocytogenes*, in relation to glandular fever, 235
 - tularensis*, intracellular parasitism and, 415
- Banana
 - diet of children, in, 262
 - maintenance of nutrition in typhoid fever, for, 221
 - preparations, infantile diarrhoea treated by, 209
- Banti's syndrome
 - aetiology, 398
 - splenectomy in, 398
- Bantus, multinucleosis among, 416
- Barberry root, antiseptic properties of, 332
- Barbiturates
 - poisoning, 409
 - antidotes, 409
 - benzedrine by intravenous drip, 346
 - sedatives, as, 332
- Basal
 - ganglia, functions of, 90
 - narcosis, 142
- Bayer 205..., 112
- Bee venom, in treatment of rheumatoid arthritis, 155
- Beethoven's deafness, 56
- Belladonna, and phenobarbitone, epilepsy treated by, 222
- Benzedrine
 - intravenous drip administration, 346
- Benzedrine sulphate,
 - dysmenorrhoea treated by, 214
 - treatment of obese children, in, 130

Benzene

- poisoning, 411
 - chronic, diagnosis of, 411
 - printers, in, 411
- Benzyl- β -dimethylamino- α -phenyl- α -ethyl-propionate hydrochloride
 - ante-spasmodic action of, 333
 - compared with papaverine, 333
- Benzyl benzoate, 112
 - scabies treated by, 391
- Berberis trifoliatis*, antiseptic properties of, 332
- Beri-beri, 26
 - alcoholic, and vitamin B deficiency, 135
 - heart, 5
- Bile-ducts, 233
 - carcinoma, extra hepatic, 234
 - common,
 - fasciola hepatica* removed from, 230
 - non-traumatic rupture of, 234
 - congenital obliteration of, 231
 - diseases, 234
- Bilharziasis, of testis, 405
- Biliary
 - cirrhosis, xanthomatous, 287
 - dyskinesia, X-ray appearance in, 233
- Birth-marks, radium therapy, 373
- Bismuth
 - anuria in infants caused by, 410
 - elimination of tissue deposits by ammonium chloride, 404
- Bites
 - human, treatment of, 269
 - stings, and, scorpions, 161
- Bituminous coal, silicosis in miners of, 389
- Black hairy tongue, 308
- Blackening-out, in aviators, 33, 34
- Bladder
 - calculi, sulphapyridine, 161
 - diseases, 161
 - effect of faeces in, 25
 - foreign bodies, 161
 - Hodgkin's disease in, 258
 - irritable, due to cervicitis, 21
 - nervous diseases, 161
 - urethral catheter in, 161
- Blast
 - injuries, 3, 10, 73, 297
 - chest complications, 297
 - clinical picture, 74
 - effect on lungs, 297
 - experimental investigations, 298
 - pathology, 73, 74
 - phrenico-costal sinus pneumonia, 298
 - treatment, 74
 - neurological effects of, 90
- Blepharitis
 - treatment,
 - brilliant green, 227
 - gentian violet and brilliant green paste, 227
- Blindness, 162
 - blood diseases causing, 162
 - degenerations and optic atrophy causing, 162
 - haemorrhage causing, 162
 - night, 5
- Blood
 - acidosis, in, 128
 - bromine content, reduction by thyroid extract, 337

INDEX

- Bone—continued**
osteoporosis, post-traumatic, treatment of, 173
Paget's disease of, 172
pseudo-fractures, 171
tumours,
malignant, 173
myeloid sarcoma, 172
myeloma,
multiple, 173
solitary, 173
non-malignant, phosphatase production in, 172
osteoclastoma, 172
Bone and joint surgery, 14
Bone marrow
examination of, 6, 7
intrasternal introduction of, in aplastic anaemia, 141
Bones
marble, 171
spotted, 171
Botulism, antitoxin treatment of, 173
Brachial plexus, origin of pain in, 189
Brain
abscess,
fungal infection and, 173
in relation to congenital heart disease, 174
alcoholism, chronic, changes in, 134
cysticercosis, radiological diagnosis of, 200
function, following cerebral injury, 85
fungal infection of, 173
localization of function, 88
tumours. *See* Cerebral tumours
vascular disorders, 175
Bran, unprepared, constipation treated with, 197
Breast
carcinoma,
mucinous, pathology of, 176
treatment of, 176
diseases of, 175
inflammation, testosterone inunction in, 175
malignant tumours of, 176
irradiation in treatment, 176
physical sign of, 176
X-ray therapy, 176
mucinous carcinoma of, 176
nipple discharge, 176
Breast feeding, 262
Brilliant green, blepharitis treated with, 227
British Pharmacopoeia, 1932
additional monographs, 112
Fourth addendum to, 112
Bromide eruptions, treatment by adrenal cortex and sodium chloride, 213
Bromides
dosage, 333
intoxication, 333
Bromine, content of blood, reduction by thyroid extract, 337
Bronchi
adenoma, 77
carcinoma, 77, 78
cardiac metastases, 294
deep X-ray therapy, harmful effects of, 372
primary, 294
Bronchi—continued
carcinoma—continued
X-ray therapy, 374
chondroma of, 294
sarcoidosis of, 295
stenosis of, as complication of asthma, 157
tumours,
malignant, 294
non-malignant, 294
Bronchial spasm, treatment by aminophylline, 158
Bronchiectasis, sinusitis, relation to, 127
Bronchiolitis, acute, 263
Bronchitis, chronic, ammonium salts as expectorants, 178
Broncho-pneumonia, 177
aspiration type, 177
clinical picture and treatment, 177
infants under one year of age, in, 178
lipid, 177
oil aspiration (lipid), 177
treatment,
sulphathiazole, 177
sulphonamide compounds, 177
young adults, in, 177
Bronchoscopy, lung abscess, in, 290
Bronchostenosis as complication of asthma, 157
Brucella
abortus, 416, 417
reaction to sulphonamides, 126
infection, associated with Hodgkin's disease, 257
Bubonic plague, sulphonamides in treatment, 99
Buccal
neuralgia, 314
spots in influenza, 263
Buerger's disease. *See* Thrombo-angiitis obliterans
Bullet
lodged in heart, 249
tissues, in, lead poisoning from, 282
Bullous reactions in Schick test, 209
Bundle-branch block, relation to cardiac enlargement, 150
Bunions, treatment of, 198
Bunyan-Stannard envelope, 114
treatment of burns, in, 180
Burns, 178
clinical picture, 178
complex systemic disturbances in, 179
encephalopathy due to, 178
first aid for, 114
first degree, 178
histopathological changes in liver, 178
liver changes in, 178
neurological after-effects, 178
pathology, 178
plasma loss in, 180, 181
shock in, 179, 180
use of adrenal cortical extract, 181
treatment of, 11, 12, 113, 179
adrenal cortical extract, 181
albucid, 182
Bunyan-Stannard envelope, 113
carron oil, 181
cod-liver oil, 181
envelope method, 180
functional aspect, 180

Burns—*continued*

- treatment of—*continued*
 - general review, 181
 - gentian violet, 181
 - glycerin-sulphonamide paste, 182
 - hospital, 179
 - local, 179
 - plasma, 180
 - plasma and serum transfusions, 181
 - plasma protein transfusion, 180
 - powdered sulphonamides, 180
 - silver nitrate, 181
 - tannic acid, 179, 181
 - war, treatment of, 179
- Bursitis
 - subacromial, 189
 - subdeltoid, 189

C

- Caecum, simple ulcers of, 193
- Caisson disease, helium-oxygen therapy, 182
- Calcareous papillitis, 312
- Calcification
 - coeliac axis, of, 153
 - renal, dissecting aneurysm secondary to, 144
 - supraspinatus tendon, in, 189
- Calcium
 - infarction, 312
 - metabolism, in toxic goitre, 236
 - plaques in kidney, 312
 - present-day diets, in, 232
- Calcium gluconate, 112
- cardiac oedema treated by, 254
- Calculus
 - pancreatic, 321
 - prostatic, trans-urethral removal, 361
 - renal, 276
 - aetiology, 276
 - containing lead, 276
 - factors in formation, 276
 - ureteral,
 - clinical picture, 276
 - surgical removal, 276
 - treatment with avertin, 276
 - vesical, sulphapyridine therapy causing, 161
- Canal of Nuck, hydrocele of, 330
- Cancer, 182. *See also* Carcinogenic agent; Malignancy; Tumours
 - aetiology, 183
 - biopsy material, quantitative examination of, 184
 - diagnosis by biochemical methods, 183
 - effects of oestrogen and androgen on cancer tissue, 183
 - mule-spinner's, 392
 - pain, relief from use of cobra venom, 184
 - pain, subarachnoid injections of alcohol for, 185
 - pathology, 183
 - sedimentation of red cells in, 163
 - treatment of, 13, 14
 - antipyretic drugs, 339
 - cobra venom, 184
 - gonad extracts, 184
 - low-temperature, 184
 - radiotherapy, 184
 - quantitative examination of biopsy material, 184
 - treatment of surrounding tissue, 185

Cancer—*continued*

- treatment of—*continued*
 - refrigeration, 350
 - uniovular and binovular twins, in, 254
- Capillaries
 - fragility and permeability, effect of vitamin P on, 426
 - intercapillary glomerulo-sclerosis and diabetes mellitus, 152
- Carbohydrate
 - dietary, high, in pulmonary tuberculosis, 293
 - metabolism and infection, 306
 - tolerance, in hypothyroidism and hyperthyroidism, 306
- Carbon disulphide, poisoning by fumes of, 411
- Carbon monoxide, poisoning, mental and neurological sequelae, 408
- Carbon tetrachloride, poisoning by, 411
- Carbuncles
 - treatment,
 - suction, 171
 - sulphathiazole, 171
- Carcinogenic agent
 - oestradiol benzoate, 183
 - oestrogenic substances, 183
 - stilboestrol, 183
- Carcinogenic effect of ultra-violet rays, 129
- Carcinoma
 - anus, of, 147, 148
 - bronchial, 77, 78, 294
 - cheek, of, 308
 - colon, of, 194
 - Fallopian tubes, of, 320
 - genital, subarachnoid injections of alcohol in, 185
 - head of pancreas, 321
 - jejunum of, primary, 272
 - liver, of, 289
 - lung, of, 294
 - mouth, of, 308
 - mucinous, of breast, 176
 - ovary, of, 319, 320
 - penis, of, 325
 - prostate, of, 361
 - rectum, of, 375
 - squamous-celled,
 - anus, of, 147, 148
 - supervening on achalasia of the cardia, 128
 - stomach, of, 400
 - tonsil, of, 349
 - ureter, of, 277, 278
- Cardiac
 - infarction. *See* Infarct
 - rupture of interventricular septum due to, 146
 - sphincter,
 - achalasia, 128
- Cardiazol. *See* Leptazol
- synonym for metrazol, 79
- Cardio-trophic properties of sex hormones, 381
- Cardiovascular
 - diseases, 1, 44
 - recruits, in, 44
 - disorders, vitamin B₁ deficiency and, 423
 - stability, and flying, 30
- Caroid, ganglion treated by injection of, 243

INDEX

- Carotid
artery, internal, aneurysm of, causing aural haemorrhage, 144
sinus, 2
- Carpal scaphoid, fractured, internal fixation of, 211
- Carriers
disinfection of hospital equipment, 185
pemphigus, neonatorum, 325
- Carron oil, burns treated with, 181
- Carrots, dermatitis caused by, 203
- Cat itch, 390
- Cataplexy, 311
- Cataract
allergic eczema and, 137
associated with tetany and osteomalacia, 186
- Cataracta tetanica, 186
- Catatonia, periodic, nitrogen balance in, 84
- Catholysis, angiomatosis retinae treated by surface diathermy and, 377
- Cauterization, chronic cervicitis treated by, 221
- Cavernous sinus thrombophlebitis, heparin and sulphonamide therapy, 408
- Cavities, tuberculous, 77
- Cavum vergae, cyst of, 175
- Centenarians, 379
- Cerebral
abscess,
fungal infection and, 173
relation to congenital heart disease, 174
concussion. *See* Concussion
cortex, thalamus and cortical activity, 89
cysticercosis, radiological diagnosis of, 200
fat embolism, triazol convulsant therapy causing, 368
hemispheres, 88
symptoms, sodium sulphapyridine therapy causing, 187
tumours, 174
acoustic neurofibroma, 174
cavum vergae, cyst of, 175
choroid plexus, stromal tumours of, 175
cyst of cavum vergae, 175
diagnosis by ventriculography and encephalography, 175
encephalography and ventriculography in diagnosis of, 175
lead encephalopathy simulating, 282
neurofibroma, acoustic, 174
stromal tumours of choroid plexus, 175
ventriculography and encephalography in diagnosis of, 175
veins,
thrombosis after childbirth, 407
thrombosis of, 92
- Cerebrospinal fever, 186
B. enteritidis infection complicating, 186
clinical picture, 186
complications and sequelae, 186
diagnosis, 65, 186
double infection, 186
meningococcal septicaemia, 186
opsonic index in, 186
prophylaxis, 65, 66, 187
sulphonamides in treatment, 65
treatment, 65, 187
sodium sulphapyridine, 187
sulphapyridine, 187
- Cerebrospinal fever—*continued*
treatment—*continued*
sulphapyridine and serum, 187
sulphathiazole, 187
Waterhouse-Friderichsen syndrome associated with, 186
- Cerebrospinal fluid
hydrochloric acid and collargol test, 188
pathology, 188
pressure, continuous recording of, 188
pressure, effect of histamine phosphate injections, 188
proteins, effect of leptazol and insulin-shock therapy, 368
- Cerebrospinal rhinorrhoea, bifrontal craniotomy, 188
- Cervical
aerocele, 311
rib, 189
- Cervicitis
chronic, treatment of, 221
irritable bladder due to, 21
- Cervico-thoracic sympathectomy, acrocyanosis treated by, 226
- Cervix uteri
carcinoma,
endometriosis associated with, 419
treatment,
local refrigeration, 419
radium and X-rays, 419
X-ray therapy, 373
failure of dilatation of os, 279
obstructions in, 279
- Chancroid, 109
treatment by sulphanilamide, 189
- Cheek, carcinoma of, tobacco chewing and, 308
- Cheilitis, lip-stick causing, 203
- Chemotherapy. *See also* Sulphonamides
acute osteomyelitis, in, 172
general paralysis of insane, in, 315
gonorrhoea, in, 237, 238
hypertension associated with renal disease, 165
intra-peritoneal infections, in, 13
laryngo-tracheobronchitis, 281
otolaryngology, in, 216
otology and laryngology, in, 56
penicillin, 338
serum therapy in pneumonia, and, 354, 355
tropical diseases, in, 99
war wounds, of, 10, 11
wound infection, 265
- Chest
blast injury to, 3
emphysematous form of, 219
significance of small intracutaneous vein on, 421
wounds and injuries, 71
treatment of, 72, 75
- Cheylietella parasitivorax*, 390
- Chicken-pox
acute pemphigus complicating, 189
herpes zoster and, 255
neurological complications, 189
- Child
adiposity in, 130, 131
banana in diet, 262
diseases of, 48

- Child—*continued*
 feeding of, 262
 glomerulo-nephritis, acute, in, 313
 Guillani-Barré syndrome, 315
 hypertension, essential, in, 164
 lead encephalopathy in, 282
 nutrition of, 49
 obese, treatment, 130
 oxyuriasis in, 311
 peptic ulcer in, 326
 pneumonia in, 355
 psychiatry of, 362
 rheumatic fever in, 377
 Chlorinated hydrocarbons, poisoning by, 411
 Chloroma, 285
 Chlorophyll, antiseptic action of, 333
 Chlorosis, 139
 Cholecystitis
 acute, aneurysm of coeliac artery simulating, 143
 visualization of gall-bladder by gas, 234
 Cholecystography, 234
 Cholesterol, serum level, effect of X-rays on, 372
 Cholesterosis of gall-bladder, 233
 Choline
 derivatives, in asthma, 333
 hydrochloride, erythraemia treated by, 225
 member of vitamin B₃ complex, as, 423
 Chondroma, of bronchus, 294
 Chorea, fever therapy and vitamin B in, 189
 Choreo-athetosis, familial paroxysmal, 159
 Chorion-epithelioma
 diagnosis, 190
 extra-genital, in male, 190
 Chorionic gonadotrophin, 22
 Choroid plexus, stromal tumours of, 175
 Chromium trioxide, gingivo-stomatitis treated by, 307
 Chromoblastomycosis, 233
 Ciba 3714...., 117
 Cibazol, 117
 Circulation
 intrahepatic, 288
 peripheral, effect of aminophylline on, 331
 Circulatory disorders of extremities, 226
 Cirrhosis
 Hanot's unilobular, 289
 xanthomatous biliary, 287
 Climacteric, 190
 in female,
 diabetes mellitus complicating, 191
 hyperthyroidism associated with, 190
 treatment,
 endocrine therapy, 191
 oestradiol implantation, 190
 oestrin, psychotherapy, and sedation, 191
 oestrone and progesterone in diabetic cases, 191
 stilboestrol, 191
 in male, 191
 sex hormone therapy, 384
 vaginitis, treatment of, 429
 Clitoris, elephantiasis, 430
Clostridium welchii
 infections, sulphanilamide in, 341
 wounds infected by, 267
 Cobra-venom
 relief of pain due to cancer, for, 184
 Cobra-venom—*continued*
 relief of pain in carcinoma of cervix uteri, for, 419
 Cod-liver oil
 burns treated with, 181
 treatment of tuberculosis, in, 415
 Coeliac
 artery, aneurysm of, 143
 axis, calcification and X-ray appearance, 153
 disease, 26
 diagnosis, 192
 haemorrhagic diathesis associated with, 192
 hypovitaminosis of fat-soluble vitamins in, 192
 identical twins, in, 191
 treatment, synthetic vitamin K, 192
 vitamin A absorption test, 192
 vitamin K deficiency in, 192
 Colchicine, effects after partial hypatectomy, 333
 Cold. *See also* Cryotherapy
 adiponecrosis e frigore due to, 226
 effect on shock, 387
 protection against, in aviation, 35
 Colds, 193
 essential unsaturated fatty acids in treatment, 193
 intranasal vaccine spray, 193
 preventive measures, 193
 treatment, 193
 vaccines for prevention of, 193
 Colic, renal, sulphonamides causing, 346
 Coliform bacillus infections, sulphonamides in treatment, 100
 Colitis, 193
 clinical picture, 193
 ulcerative, 193
 clinical picture, 193
 lymphopathia venereum, relation to, 193
 treatment, sulphonamide compounds, 194
 Collapse, 385. *See also* Shock
 Collargol test, 188
 Colon
 abnormalities of, 231
 carcinoma of, 194
 clinical picture, 195
 incidence, 194
 multiple primary polypi, 195
 one stage resection, 195
 symptoms, 194
 treatment, 195
 diverticulitis, obstructing, 212
 polypi, multiple primary, 195
 polyposis of, 375
 simple ulcers of, 193
 triplication of, 231
 Colostomy, in obstructing diverticulitis, 212
 Colo-vesical fistula, diverticulitis and, 25
 Coma, diabetic, warning symptoms of, 207
 Compressed-air workers, aero-otitis media in, 182
 Compression injuries, 1, 9
 Concussion
 acceleration, 93
 compression, 93
 duration of paralysis, 94

INDEX

- Concussion—*continued*
 experimental, 92
 haemorrhagic lesions, 94
 influence of shape of the skull, 94
 paralytic phenomena, 94
 pulmonary, and blast, 3
 scalp wounds complicating, 196
 theory of, 195
- Conglutinatio orificii externi, 279
- Conjugal neurosyphilis, 403
- Conjunctiva
 diseases of, 196
 malignant melanoma of, 196
 tumours of, 196
- Conjunctivitis, 196
 chronic unilateral, due to virus of lympho-
 pathia venereum, 300
 inclusion, sulphanilamide therapy, 196
 inflammation,
 bacterial, 196
 non-bacterial, 196
 treatment, silver ferrihaemoglobin, 339
- Constipation, 196
 experimentally induced, 197
 treatment with unprepared bran, 197
- Contraception
 jellies, 197
 'safe period', 197
 spermicidal preparations, 197
- Convalescent
 blood, herpes zoster ophthalmicus treated
 by, 198
 serum, in prophylaxis of measles, 302
- Convulsion therapy
 ammonium chloride, 368
 anxiety states, in, 80
 compulsion neurosis, in, 364
 electric, in mental disease, 218
 electrical, 80, 368
 fractures of vertebrae caused by, 80
 insulin shock, 367, 368
 involutional melancholia, in, 79
 leptazol, 366, 367, 368
 mental disorders, in, 79
 schizophrenia, in, 79
 sub-convulsant doses in, 365
 triazol, 368
- Convulsions
 infantile,
 sodium diphenyl hydantoinate in treat-
 ment, 197
 treatment of underlying causes, 197
 otogenic origin, of, 216
- Cooley's erythroblastic anaemia, 140
- Cor
 bi-atriatum triloculare, 248
 pulmonale,
 chronic, 291
 subacute, 252
- Coramine, 112
 effect on abnormal respiratory rate, 334
 heart disease, in, 334
- Cornea
 examination by means of fluorescein,
 226
 herpes zoster, convalescent blood in treat-
 ment, 198
 hypopyon, treated by sulphonamides, 198
 opacities, intravenous injections of as-
 corbic acid in, 198
- Cornea—*continued*
 ulcer,
 treatment,
 intravenous injections of ascorbic
 acid, 198
 sulphonamides, 198
 use of fluorescein in various conditions,
 226
- Corns, soft, treatment of, 198
- Coronary
 arteries, rupture, 144
 disease,
 tobacco smoking and, 152
 X-ray diagnosis of, 146
 occlusion, 145. *See also* Coronary throm-
 bosis
 thrombosis, 144
 coronary occlusion and, 145
 course and prognosis, 145
 diagnosis, 146
 mortality, immediate, 145
 pain, 145, 146
 premonitory symptoms, 145
 prodromal pain, 145
 rehabilitation, 146
- Coroner
 appointment and qualifications, 199
 fees at inquests, 199
- Corpus callosum, agenesis of, 174
- Cortin
 pneumonia treated by sodium chloride
 and, 355
 pre-operative administration of, 387
- Corynebacterium diphtheriae*
 diffusing factor and substance B, 209
 soluseptasine and M & B 693, action of,
 341
 virulence test, 209
- Cottunometer, continuous recording of cere-
 brospinal fluid pressure by, 188
- Craniolacunia, associated with meningocele,
 396
- Craniotomy, bifrontal, for cerebrospinal
 rhinorrhoea, 188
- Crohn's disease, 199
 clinical picture, 199
 metabolism in, 200
 radiology, 199
- Cross infection, 13
- Crush
 injuries, 1
 prolonged compression of limbs,
 269
 treatment, 269
 syndrome, 1, 9, 269
 impairment of renal function in,
 269
- Cryotherapy, in acne vulgaris, 129
- Cyanose tardive*, 248
- Cyanosis, sulphonamides producing, 115
- Cyst
 cavum vergae, of, 175
 dermoid. *See* Dermoid cyst
 nasal septum, of, 204
 gas, of intestine, 272
 pancreatic, 321
- Cysticercosis
 cerebral, difficulty of radiological detec-
 tion, 200
 epilepsy, 222

INDEX

- Cysticercus cellulosae*, incidence and detection in man, 200
- Cystine, effect on lactation, 262
- hydrochloride, infected wounds treated by, 268
- D
- Da Costa's syndrome, 2, 244, 245
- Dacryocystitis, of new-born, treatment of, 281
- Darier's disease, vitamin A therapy in, 200
- Dark-adaptation, prolonged, in obstructive hepatic jaundice, 273
- Deaf, education of, 52
- Deaf-mutes, mental capacity of, 53, 54
- Deafness
- aviators, in, 160
 - Beethoven's, 56
 - chronic, prostigmin in, 201
 - diagnosis, 201
 - effect of certain lesions, 55
 - mode of onset, 55
 - otosclerosis and, 201
 - psychological effects of, 52
 - psychological reactions, 201
 - treatment, 201
 - prostigmin, 201
 - prostigmin methylsulphate, 201
 - round-window grafts, 201
- Decicain, 113
- Dehydrating agent, sorbitol as, 339
- Dehydration, blood changes in, 128
- Dementia
- praecox. *See* Schizophrenia
 - pre-senile, 84
- Dental sepsis
- complications after extraction of teeth, 202
 - neurological complications, 202
 - short-wave therapy, 202
- Dentition, abnormal, 202
- Dermatitis, 202
- arsenical, herpes simplex associated with, 256
 - arsphenamine causing, 332
 - carrots causing, 203
 - ethyl mercury phosphate causing, 203
 - exfoliative,
 - fatal case, 204
 - naphthalene causing, 204
 - phenobarbitone causing, 204
 - gentian violet causing, 203
 - herpetiformis, sensitization to halogens and bacterial allergens, 204
 - iroko wood causing, 203
 - irradiation, surgical treatment of, 202
 - nail polish causing, 203
 - plants causing, 202
 - plants, irritating, 202
 - poison ivy causing, 203
 - pyrethrum causing, 202
 - radio-, surgical treatment of, 202
 - toxic, 202
 - plants, irritant, 202
 - pyrethrum, 202
 - woods, irritant, 203
 - venenata, 203
 - sulphonated oil as detergent in, 203
- Dermatofibroma, 393
- Dermato-myositis, 309
- compared with systemic lupus erythematosus, 309
 - complications, 309
 - metabolic disturbances in, 309
 - relation of progressive scleroderma to, 379
- Dermatophytosis pedis*, 233
- Dermatoses, sulphapyridine in, 342
- Dermoid cyst
- congenital, of nasal septum, 204
 - of ovary,
 - malignant, 320
 - traumatic rupture of, 319
- Derris elliptica*, 391
- Derris root, scabies treated by, 391
- Desoxycorticosterone
- acetate,
 - cardiac failure after, 132
 - embryo implantation, effect on, 335
 - endometrium, effect on, 335
 - implantation in Addison's disease, 131
 - oestradiol for normal infants, and, 335
 - sublingual administration in Addison's disease, 131
 - uraemia treated with, 417
 - prevention of fibromyomas after oestrogen injections by, 383
- Dextrin-maltose-dextrose carbohydrate, use in infant feeding, 262
- Dextrocardia, 246
- Diabetes insipidus, 205
- treatment,
 - pitressin tannate, 205
 - total thyroidectomy, 205
- Diabetes mellitus, 205
- aetiology, 205
 - aneurin administration in, 206
 - ascorbic acid in, 206
 - blood-sugar in, 207
 - clinical picture, 205
 - coma, warning symptoms of, 207
 - complicating menopause, 191
 - complications, 205, 206
 - diagnosis, 206
 - insulin, 206
 - intercapillary glomerulo-sclerosis and, 152
 - nephrotic syndrome with hypertension in, 205
 - pancreatitis, acute haemorrhagic, complicated by, 321
 - pellagra-like condition in, 206
 - pituitary anti-diabetogenic principle, 205
 - pregnancy, in, 16
 - pre-operative procedure in, 207
 - symmetrical peripheral neuropathy in, 206
 - treatment, 206
 - aneurin and riboflavine, 206
 - ascorbic acid, 206
 - insulin-quinine, 207
 - pre-operative procedure, 207
 - thiamin, 422
 - zinc protamine insulin, 206
 - tuberculosis associated with, 205
 - zinc protamine insulin in, 206
 - vitamin B, deficiency in, 422
 - vitamin C nutrition in, 425
 - vitamin therapy, 206
 - Wesselow and Griffiths' test, 206
 - zinc protamine insulin, 206

INDEX

- Diabetic
coma, warning symptoms of, 207
retinitis, varices in, 376
- Diamidines in protozoal infections, 100
- 4 : 4'-Diamidinostilbene
kala-azar treated by, 274
trypanosomiasis treated by, 413
- Diaphragm, paroxysmal flutter of, 207
- Diarrhoea
flagellate infection and, 208
giardia infection and, 208
treatment with atebirin dihydrochloride, 208
- infantile, 208
biochemistry, 208
treatment,
banana preparations, 209
sulphathiazole, 208
vitamin C excretion in, 208
vitamin deficiency diseases due to chronic, 208
- Diastase, low blood, 163
- Diathermy, angiomas retinae treated by
catholysis and, 377
- Dick test, reliability of, 261
- Diet
amino-acids in, 232
calcium in, 232
carbohydrate, in pulmonary tuberculosis, 293
minimum optimum requirements, 232
peptic ulcer, in, 328
- Dietetic deficiencies, 209
- diarrhoea, chronic, causing, 208
- Diethylstilboestrol, vaginitis, post - meno -
pausal, treated by, 429
- Digilanid, effect on heart, 334
- Digitalis, heart failure treated by ouabaine
and, 254
- Digitalis*
lanata, 334, 337
purpurea, 334, 337
- Dihydrotachysterol, pemphigus vulgaris
treated by, 324
- Dilantin
sodium. *See* Sodium diphenylhydantoinate
poisoning by, 409
soluble, 113
- Diphtheria, 209
antitoxic serum, analysis of, 260
antitoxin,
'anti-B' factor in, 209
level in pregnancy, 260
bacteriology and pathology, 209
diagnosis, 66
formol toxoid in treatment of leprosy, 284
glandular fever simulating, 235
immunization against, 4
immunization against tetanus and, 260
prophylaxis, 66, 67
Schick test, bullous reactions, 209
toxoid injection, end-results of, 210
treatment, 66
antitoxin, 209
vitamin B₁, 210
vagina, of, 429
viability and air-borne infection, 209
virulence test, 209
- Dislocations, 210
- Disseminated sclerosis
artificial fever therapy, 212
treatment by artificial fever, 212
- Diuretics, mercurial, in heart failure, 253
- Diverticulitis, 212
colo-vesical fistula and, 25
obstruction and colostomy, 212
- Diverticulosis, 25, 212
- Diverticulum
duodenum, of, 212
stomach, of, 402
- Dolantin, 113
- Dolantol, 113
- Dressings
petroleum jelly, 264
tulle gras, 263
- Drowning, resuscitation, 212
- Drug eruptions, 213
arsphenamines, purpura haemorrhagica
due to, 213
bromide, 213
purpura haemorrhagica due to arsphenamines, 213
sulphapyridine, 213
- Drug therapy, recent developments in, 111
- Drugs
antipyretic, 339
economy in, 111
Fourth Addendum to *British Pharmacopoeia*, 112
injections, 112
nasal mucosa, action on, 331
National War Formulary, 112
new official substances, 112
nose, for, 334
Pharmacy and Medicines Act (1941), 111
proprietary, names of, 113
rectal administration of, 339
reduction of heat by, 339
shortage and the war, 111
skin, action on, 331
sterilization methods, 113
substances of German origin, 112
sympathomimetic and parasymphomimetic, 346
- Ductus arteriosus
patent, 2
left ventricular compensation, 247
surgical treatment, 247
- Duodenal
atresia, congenital, 272
ulcer, 326. *See also* Peptic ulcer
treatment, partial gastrectomy, 326, 327
tuberculous, perforation of, 326
- Duodenum
atresia of, congenital, 272
diverticulum, peri-vaterian, 212
sprue, in, 27
tuberculous ulcer, perforation of, 326
- Dupuytren's contraction, microscopic investigation, 213
- Dust, diphtheria bacilli in, 209
- Dust-borne organisms, in hospital wards, 185
- Dysentery
amoebic, skin manifestations of, 138
bacillary,
treatment
sulphanilylguanidine, 213, 65
sulphapyridine, 118
diagnosis, 64

INDEX

- Dysentery—*continued*
 sulphonamides in treatment, 65
 treatment, 65
- Dyskinesia, biliary, X-ray appearance in, 233
- Dysmenorrhoea, 214
 aetiology, 214
 implantation of progesterone, 384
 treatment by benzedrine sulphate, 214
 uterine contractions and, 214
- Dyspepsia, 4
- Dyspnoea, vitamin B₁ therapy in, 254
- Dystrophy
 muscular. *See* Muscular dystrophy
 vitamin B₆ therapy, 428
 vitamin E therapy, 5, 426, 428
- E
- Ear
 diseases, 52, 216
 chemotherapy in, 56
 haemorrhage, caused by aneurysm of internal carotid, 144
 middle. *See* Middle ear
- Eclampsia
 hypertension and, 18
 renin and, 18
 veratrum viride therapy, 358
- Ecthyma contagiosum, 217
- Ectodermal dysplasia, familial incidence, 147
- Eczema
 allergic, and cataract, 137
 infantile, 137
- Effort syndrome, 2, 46, 244
 aetiology, 244
 clinical picture, 244
 general review, 244
 personality types and, 245
- Ehlers-Danlos syndrome, 230
- Eighth nerve, affections of, 199
- Electric shock therapy, in mental disease, 218
- Electrical convulsant therapy, in mental disorders, 368
- Electrical convulsions, in treatment of mental disorders, 80
- Electrical injury, clinical effects of, 217
- Electrocardiogram
 Adams-Stokes attacks and, 246
 effects of fear on, 149
 hypertension, in, 245
 multiple chest-lead, in pulmonary embolism, 296
 strophantin and glucose, effects of, 340
 T wave inversion, 245
- Electro-encephalography
 diagnosis of cerebral tumour, in, 175
 epilepsy, in, 91
- Electrolytes, blood, and menstrual cycle, 163
- Electrotherapy, 217
 direct current, 217
 high-frequency currents, 217
 ionization, 217
 low-voltage varying currents, 218
 magnetism, importance of, 217
- Elephantiasis
 clitoris, of, 430
 penis and scrotum, of, 325
- Embolectomy, 218
- Embolism
 arterial, 218
 embolectomy, 218
 mural thrombi as source of, 218
 prevention of gangrene of extremity, 218
 cerebral fat, triazol convulsant therapy causing, 368
 fat, 1, 74, 75
 shock and, 386
 triazol convulsant therapy causing, 368
 mesenteric, 125
 pneumothorax caused by, 290
 pulmonary, 74
 diagnosis by multiple lead cardiograms, 296
 heparin therapy, 296, 297
 incidence and occurrence, 295, 296
 ligation of femoral veins for prevention, 296
 operative prevention, 296
 post-operative, 295
 predisposing conditions, 295
 treatment, 296
- Embryo, implantation, effect of desoxycorticosterone acetate, 335
- Embryotomy, 279
- Emphysema
 acute, operative treatment of, 219
 pulmonary,
 chronic obstructive, 219
 form of chest in, 219
 functional impairment and, 219
 tuberculous obstructive, in children, 219
- Encephalitis,
 epidemica, 219
 differentiation of viruses, 220
 Parkinsonism, treatment by syntropan, 220
 treatment,
 β -erythroidine hydrochloride, 332
 syntropan, 220
 measles complicated by, 302
- Encephalography, diagnosis of cerebral tumour, in, 175
- Encephalo-myelitis
 acute disseminated, 220
 due to toxoplasma, 220
 new conceptions and allied forms, 220
- Encephalopathy
 arsphenamine causing, 332
 burns causing, 178
 lead, in children, 282
 lead, simulating cerebral tumour, 282
 sulphamethylthiazole therapy causing, 175
- Endocarditis
 atypical verrucous, 250
 combined with lupus erythematosus, 250
 bacterial, treatment, sulphonamides, 118
 gonococcal septicaemia associated with, 237
 malignant, 249
 meningococcal, 250
 streptococcus viridans infection, 250
 subacute bacterial, 2, 249
 aetiology, 249

INDEX

- Endocarditis—*continued*
 subacute bacterial—*continued*
 bacteriology, 251
 clinical picture, 250
 effects on nervous system, 250
 meningococcal infection without meningitis, 250
 streptococcus viridans infection with recovery, 250
 streptococcus viridans infection, treatment, 251
 syphilitic aortic valvulitis, after, 249
 treatment, 251
 heparin, 251
 sulphapyridine, 251
 sulphapyridine and heparin, 251
 syphilitic, 249
- Endocrine therapy. *See* Hormone therapy
- Endocrinology, 4, 5
- Endometrial
 extract, 383
 transplants, lungs, in, 221
- Endometriosis, 221
 associated with carcinoma of cervix, 419
 endometrial transplants in lungs, 221
 morbid anatomy and pathogenesis, 221
 recto-vaginal septum, of, 221
 treatment by testosterone propionate, 221
- Endometrium, desoxycorticosterone acetate, effect of, 335
- Endotoxoid
 Grasset's tubercle,
 lupus vulgaris treated by, 300
 treatment of leprosy, in, 284
- Entamoeba histolytica*, amoebiasis cutis caused by, 138
- Enteric fevers, 221
 combined immunization against tetanus and, 407
 diagnosis, 63
 prophylaxis, 64
 T.A.B.C. vaccine in, 261
 treatment, 63, 64
- Enterobiasis, children, in, 312
- Enterobius vermicularis*, 312
- Enterocolitis, ulcerative, phenolphthalein test in, 273
- Envelopes, Bunyan-Stannard, in treatment of burns, 114, 180
- Enzyme, proteolytic, in treatment of ganglion, 243
- Eosinophilia
 pulmonary, 157
 tuberculous pleuritic effusion, in, 291
- Epanutin, 113
- Epidemiology, present war, 62
- Epidural abscess, diagnosis of, 397
- Epilepsy, 222
 aetiology, 222
 benign hyperplasia of gums in, 222
 cysticercosis, cerebral, and, 200, 222
 electro-encephalography in, 91
 treatment,
 children, in, 222
 phenobarbitone and belladonna, 222
 sodium diphenylhydantoinate, 222, 223
 vitamin C deficiency in, 222
- Epithelioma
 multiple benign cystic, 393
 vulva, of, 430
- Epituberculosis, differential diagnosis from Löffler's syndrome, 157
- Eptoin, 113
- Ergometrine, in treatment of normal puerperium, 370
- Ergot, alkaloids, thyrotoxicosis treated by, 236
- Ergotamine, thyrotoxicosis treated by, 236
- Ergotoxine, thyrotoxicosis treated by, 236
- Eruptions, anomalous and atypical, 223
- Erysipelas, treatment by sulphanilamide, 224
- Erythema, 224
 clinical picture, 224
 due to external causes, 224
 due to internal causes, 224
 livedo reticularis, 224
 multiforme, 224
 nodosum, associated with tuberculosis, 224
 scarlatiniforme, 224
- Erythraemia
 circulatory adjustments in, 225
 clinical picture, 225
 thrombosis complicating, 225
 treatment,
 lipocatac and choline, 225
 vitamin C and sodium bicarbonate, 225
- Erythroblastaemia, 141
- Erythroblastic anaemia, 140
- Erythroblastosis, 140, 141
 vitamin K therapy, 141
- Erythrocyanosis, 226
 clinical picture, 226
 treatment, 226
- Erythrocytes. *See* Blood cells
- Erythromelalgia, 226
- Erythrophagocytic anaemia, 140
- Ethyl mercury phosphate, dermatitis caused by, 203
- Eumydrin
 hypertrophic pyloric stenosis treated by, 370
 pyloric stenosis treated by, 4, 13, 50
- Eunuchism, treatment by testosterone and testosterone propionate, 384, 385
- Eventration, 255
- Evipan
 anaesthesia, investigation of neuroses by, 259
 sodium. *See* Hexobarbitone soluble
 narcosis in tetanus, 407
 soluble, in labour, 280
- Evisceration, obstetric, 279
- Exercise tolerance test, 44, 244
- Exophthalmic ophthalmoplegia, 319
- Expectorants, ammonium salts as, 178
- Extra-dural abscess. *See* Abscess
- Extrasystoles, treatment, potassium chloride, 150
- Extremities
 arterial diseases, 151
 vascular diseases, 151
- Eye
 diseases,
 silver ferrihaemoglobin in, 339
 sulphonamides in, 118, 342
 examination of, 226
 cornea, 226
 fundus, 227
 pain, retrobulbar injection of proctocaine for, 244
 percaïne, sensitivity to, 338

INDEX

- Eyelids
inflammation, 227
injuries and diseases, 227
- F
- Face
nodular syphilide of, 403
powder, removal of, 334
- Facial paralysis, herpes zoster and, 256
- Faeces
effect of faeces in, 25
soiling of perianal skin by, 147
toxic factor in poliomyelitis, 356
- Fallopian tubes
carcinoma,
diagnosis, 228
origin in uterus, 228
primary, 228
treatment, 320
diseases, 228
infection and ectopic pregnancy, 228
insufflation, in sterility, 399
tumours, 228
- Familial incidence
choreo-athetosis, paroxysmal, 159
ectodermal dysplasia, congenital, 147
haemolytic anaemia, 139
haemorrhagic telangiectasia, 223
jaundice, non-haemolytic, 141
oedema of legs, persistent, 318
purpura simplex, 241
- Faradic shock therapy
acute mania, in, 365
mental disorders, in, 368
- Faradism, used for shock-therapy in mental disease, 218
- Fasciola hepatica*, removed from common bile-duct, 230
- Fascioliasis, treatment of, 230
- Fat
absorption, mechanics of, 26
embolism, 1, 74, 75
shock and, 386
triazol convulsant therapy causing, 368
lymphatic glands in, 300
- Fatigue
aviators, in, 35
muscular, effect of amino-acetic acid and gelatin on, 331
- Fatty acids, essential unsaturated, common cold treated by, 193
- Fear, effects on electrocardiogram, 149
- Feminism, hyperfunction of adrenal cortex, in, 133
- Femoral veins, ligation for prevention of pulmonary embolism, 296
- Femur
fracture of, 14
fracture of neck, convulsion therapy causing, 366
- Fever, as initial symptom of renal tumour, 277
- Fibrillation
auricular. *See* Auricular fibrillation
muscular, peripheral origin, 229
ventricular. *See* Ventricular fibrillation
- Fibroma, nasopharynx, of, 317
- Fibromyoma
prevention after oestrogen injections, 383
uterus, irradiational treatment, 419
- Fibrosis, hepato-lienal, 398
- Fibrositis, 229
diagnosis and differential diagnosis, 229
treatment, 229
heat and Scott's dressing, 229
injection of local anaesthetic, 229
vitamin E, 230
- Fistula
arteriovenous,
diagnosis of, 421
treatment of, 422
colo-vesical, and diverticulitis, 25
gastro-colic, 329
gastro-jejuno-colic, 329
jejunocolic, nutritional oedema due to, 318
vesico-vaginal, operation for, 430
- Flagellate infections, diarrhoea associated with, 208
- Flocculation test, Meinicke, in tuberculosis, 414
- Fluke infections, intestinal, 230
- Fluorescein, corneal examination, in, 227
- Fluorine, geological distribution in relation to endemic goitre, 235
- Flying. *See also* Aviation medicine
aptitude for, 29
aptitude test, 29
cardiovascular stability, 30
effect of altitude changes on intracranial volume, 160
high-altitude, fitness for, 30
hyperventilation in, 159
night vision, 30, 31
night visual capacity, 30, 31
pre-selection of men for, 29
psychological pre-selection of personnel, 32
stereoscopic vision, 31
- Foetus, 230
abnormalities, 230
digestive system, 230
genito-urinary system, 230
skin, 230
anonychia, partial, with bony changes, 230
ascites, obstructed labour due to, 279
bile-ducts, congenital obliteration of, 231
colon, triplication of, 231
Ehlers-Danlos syndrome, 230
monorchia, 231
testis, absence of, 231
- Food, 231
calcium, 232
minimum optimum requirements, 232
nitrogenous constituents, 232
poisoning, 232
simple dietaries, 232
- Foot
deformities of, 232
dermatophytosis, 233
diseases of, 232
diseases, and military service, 232
fracture, bilateral march, 211
gangrene of, complicating scarlet fever, 378
pain, in acromegaly, 129
ringworm, 233
supernumerary metatarsal bone, 232
- Foreign bodies
bladder, in, 161
heart, in, 249
X-ray examination, 371

INDEX

- Formol-gel reaction, diagnosis of rheumatic diseases, in, 154
- Fouadin, ulcerative granuloma treated by sulphapyridine and, 239
- Fractures, 210
 ankle joint, osteoarthritis complicating, 211
 carpal scaphoid, internal fixation of, 211
 compound, treatment by closed plaster method, 267
 convulsion therapy causing, 366, 367
 femur, of, 14
 foot, 211
 internal fixation in conjunction with sulphanilamide, 210
 leptazol shock therapy causing, 366
 march, bilateral, 211
 olecranon, of, 14
 pseudo-, 171
 skull, and injury to posterior pituitary, 174
 splintage, use of vitalium, 210
 treatment,
 internal fixation in conjunction with sulphanilamide, 210
 vitalium appliances, 210
 union, rôle of oestrogen, 211
 wrist joint, 211
- Fragilitas ossium, idiopathic, 171
- Frei's test, 109
- Friedman test, positive results in non-pregnant states, 358
- Frontal
 leucotomy,
 technique, 82
 treatment of mental disorders, in, 81, 82
 lobe, symptom-complexes associated with lesions of, 174
- Frost-bite, aviators, in, 35
- Fruit juice, effect on gastric function, 259
- Fundus oculi, importance of reflexes of, 227
- Fungicidal dusts, poisoning from inhalation of, 411
- Fungous
 diseases, 233
 skin allergy due to, 137
 infection, brain, of, 173
- Furfuryl trimethyl ammonium iodide, intravenous drip administration, 346
- G
- Gall-bladder, 233
 cholesterosis of, 233
 function, disturbance of, 233
 giardial infection, 24
 physiology, 233
 roentgenography, 234
 strawberry, 233
- Gall-stones, 233
 ileus, recurrent, 125
 intestinal obstruction due to, 125
- Ganglion
 injection treatment, 243
 X-ray treatment, 243
- Ganglioneuroma, mediastinum, of, 303
- Gangrene
 feet, of, complicating scarlet fever, 378
 gas, sulphanilamides in, 341
 skin, of, progressive, 392
- Gas
 cysts, intestine, of, 272
 gangrene, sulphanilamides in, 341
 poisoning, 408
- Gastrectomy, 14
 partial, for peptic ulcer, 326
 total,
 partial oesophagectomy, and, 401
 technique, 401
- Gastric
 acidity,
 gastric resection and, 327
 nicotine, effect of, 326
 changes following injury to posterior pituitary, 174
 function, effect of fruit juice on, 259
 lavage, pulmonary tuberculosis, in, 292
 mucosa
 effect of alcohol on, 135
 presence of spirochaetes in, 401
 secretion, depressant effect of carcinoma extracts on, 401
 ulcer. *See also* Peptic ulcer
 alkali poisoning in, 135
 presence of spirochaetes in gastric mucosa, 401
 treatment, vitamin A (avoleum), 327
- Gastritis
 alcoholism causing, 135
 syphilis in relation to, 234
- Gastro-colic fistula, 329
- Gastro-enteritis
 acidosis associated with, 128
 blood changes in, 128
- Gastro-intestinal
 allergy, milk as cause of, 138
 disease, incidence during the war, 215
 haemorrhage, transfusion of whole blood in, 169
 symptoms,
 old age, in, 380
 pulmonary tuberculosis, in, 292
 tract, ulceration, phenolphthalein test in, 273
- Gastro-jejunal ulcer, 328
 clinical picture and morbid anatomy, 328
 gastro-colic and gastro-jejuno-colic fistula complicating, 329
- Gastro-jejuno-colic fistula, 329
- Gastrosocopy, 3, 4
- Gaucher's disease
 biopsy examination of pingueculae, 287
 diagnosis by sternal puncture, 287
- Gelatin, effect on muscular fatigue, 331
- General paralysis of the insane, 315
 treatment, 315
 artificial fever and malaria therapy compared, 315
 combined artificial fever, chemotherapy, and vaccino-therapy, 315
 pyretotherapy, 105
- Genital, cancer, subarachnoid injections of alcohol in, 185
- Genito-urinary tract, *trichomonas vaginalis* infestation in male, 417
- Gentian violet
 blepharitis treated with, 227
 burns treated with, 181
 dermatitis caused by, 203

INDEX

- Giant-celled tumour, bone, of, 172
Giardia intestinalis, 24
 infestation, diarrhoea associated with, 208
 Giardiasis, 24
 clinical picture, 24
 diarrhoea associated with, 208
 treatment, 24
 Gingivitis
 ascorbic acid in treatment, 308
 short-wave therapy in, 202
 treatment by chromium trioxide, 307
 Glandular fever, 235
 aetiology, 235
 agglutination tests, 235
 angina of throat associated with, 235
 blood picture, atypical, 235
 clinical picture, 235
 complications, 235
 differential diagnosis, 235
 Paul-Bunnell test in, 235
 simulating diphtheria, 235
 splenic rupture in, 235
 treatment, sulphapyridine, 118
 Glare, affecting eyes of aviators, 36
 Globus pallidus, functions of, 90
 Glomerulo-nephritis, 312
 acute,
 children, in, 313
 hypertension and, 312
 treatment by magnesium sulphate, 312
 children, in, 313
 chronic, calcium plaques in, 312
 clinical picture, 313
 course and prognosis, 313
 Glomerulo-sclerosis, intercapillary, and diabetes mellitus, 152
 Glomus tumours, 393
 nail, of, 311
 synovial membrane of knee, on, 393, 394
 Glossitis, vitamin deficiency in, 424
 Glucose
 hypertonic injections, in cardiac disease, 340
 tolerance, and staphylococcal infection, 306
 Glutamic acid, effect on lactation, 262
 Gluteus medius muscle, defect of, postural treatment, 310
 Glycerin-sulphonamide paste, burns treated with, 182
 Glycine, effect on lactation, 262
 Goitre, 235
 endemic, fluorine and, 235
 simple, geological distribution of fluorine in relation to, 235
 toxic, 236
 calcium and phosphorus metabolism, 236
 clinical picture, 236
 excretion of hippuric acid in, 236
 pathology, 236
 treatment, ergot alkaloids, ergotamine and ergotamine, 236
 Gold compounds, in treatment of rheumatoid arthritis, 154
 Gonad extracts, malignant disease treated by, 184
 Gonadotrophic hormone. *See* Hormone therapy; Hormones
 chorionic, undescended testis treated by, 406
 undescended testis treated by, 406
 Gonadotropius, pituitary, synergism of oestrogens with, 384
 Gonococcal septicaemia
 associated with endocarditis, 237
 treatment, 238
 Gonorrhoea, 107, 237
 bacteriology, 237
 diagnosis, 107
 diagnostic cutaneous test, 237
 males, in,
 treatment, 237
 albucid, 237
 sulphapyridine, 237, 238
 sulphathiazole, 237
 sulphathiazole and sulphamethylthiazole, 238
 sulphathiazole and sulphapyridine, 238
 toxic effects of sulphathiazole, 238
 pathology, 237
 salpingitis, oestrogenic therapy, 228
 treatment,
 artificial fever and chemotherapy, 238
 sulphapyridine, 117
 sulphathiazole, 107
 sulphonamide compounds, 107, 108
 sulphonamides with pyrexial treatment, 108
 Gordon's reaction, Hodgkin's disease, in, 258
 Gout, diagnosis and differential diagnosis of, 239
 Grafting, skin, 264
 Granuloma
 inguinale, 109
 traumatic, of synovial membrane, 274
 ulcerative, treatment, sulphapyridine with fonadin, 239
 Granulomatosis, lipoid. *See* Schüller-Christian syndrome
 Granulosa and theca-celled tumours of ovary, 320
 Grasset's tubercle endotoxoid
 leprosy treated with, 284
 lupus vulgaris treated by, 300
 Growth hormone, 351
 Guillain-Barré syndrome, 315
 Gum acacia, as cause of asthma, 157
 Gums
 benign hyperplasia of, in epileptics, 222
 hypertrophy of, 230
 Gynaecology, advances in, 16
 Gynaecomastia
 stilboestrol as cause of, 383
 symptom of extra-genital chorion-epithelioma, 190
- ## H
- Haemangioma
 scrotum, of, 325
 uterus, of, 419
 Haematemesis, blindness after, 162
 Haematology, advances in, 6, 7
 Haematoma, sarcoma arising from, 183
 Haematoporphyria, acute, complicated by acute polyneuritis, 239

INDEX

- Haematuria**
hypernephroma causing, 277
sulphathiazole causing, 240
sulphonamides causing, 346
sulphonamides producing, 116
- Haemochromatosis**, anomalous symptoms in, 240
- Haemoglobin**, 7
fate of extra-corpuscular circulating, 170
injections of, 170
- Haemoglobinaemia**, 170
paroxysmal nocturnal, 140
- Haemoglobinuria**
chronic haemolytic anaemia with, 140
sulphanilamide causing, 240
- Haemolysis**, intravascular, 7
- Haemolytic anaemia**. *See* Anaemia, haemolytic
- Haemophilus influenzae**
adrenal haemorrhage caused by, 132
meningitis caused by, 305
- Haemoptysis**, Hodgkin's disease, in, 258
- Haemorrhage**
adrenal,
acute bilateral, 132
meningococcal septicaemia associated with, 186
pregnancy, in, 358
allergy induced by anti-haemorrhagic substances, 170
associated with familial haemorrhagic telangiectasia, 223
aural, caused by aneurysm of internal carotid, 144
blindness after, 162
gastro-intestinal, blood chemistry in, 139
gastro-intestinal, transfusion of whole blood in, 169
hypoprothrombinaemic, after operation for appendicitis, 149
intravenous injections of sodium ascorbate, 269
new-born, in, vitamin K therapy, 427
petechial, anti-syphilitic therapy causing, 405
transfusions of isinglass, 269
- Haemorrhagic**
deficiency disorders,
plasma-prothrombin titrations in infants, 241
treatment by vitamin P, 241
- diathesis**,
associated with idiopathic steatorrhoea, 192
pathogenesis and morbid anatomy, 241
primary non-hereditary, 241
diseases, 241
hereditary, 241
telangiectasia, familial, 223
- Haemorrhoids**, internal, injection treatment, 375
- Haemostasis**, mechanism of, 268
- Haemothorax**
traumatic, 72, 73
treatment of, 242
- Hair**
permanent waving, hydrogen sulphide poisoning, 410
red, and susceptibility to tuberculosis, 414
- Hair follicles**
abnormalities and diseases, 243
tumours derived from, 393
- Halogens**, sensitization to, in dermatitis herpetiformis, 204
- Hand**
diseases and deformities, 243
ganglion of, 243
Heberden's nodes, 243
osteophytes, 243
pain, in acromegaly, 129
ringworm, 233
- Hand-Schüller-Christian syndrome**. *See* Schüller-Christian syndrome
- Hanot's unilobular cirrhosis**, 289
- Hay fever**
effect of pollen contact on age of onset, 137
pollen extracts and skin sensitivity, 137
treatment,
oral pollen, 137
slow absorbing pollen extract, 136
- Headache**, 90, 91, 244
hypertension, relation to, 306
migraine, of, 91
powders, poisoning by, 409
- Healing**, wounds, of, 113
- Hearing**
aviators, of, 160
effect of aircraft noise on, 36
- Heart**
abnormalities, congenital, 246
acetylcholine, effect of, 333
auscultation, portable amplifier for, 245
beri-beri, 5
bullet lodged in, 249
carcinoma, secondary to carcinoma of bronchus, 294
dextrocardia, 246
digilanid, effect of, 334
disease, 44, 244
associated with rheumatoid arthritis, 154
congenital, 246
cerebral abscess in relation to, 174
recruits, in, 44
syphilis, congenital, incidence of, 403
traumatic, 270
vitamin B₁ deficiency and, 423
disordered action of, 2
disorders,
coramine, effects of, 334
hypertonic glucose injections in, 340
pitressin, effects of, 336
respiration in, 334
effect of fear on, 149
effect of sex hormones on, 381
enlargement, relation of bundle-branch block to, 150
examination of, 244, 245
foreign bodies, 249
functional capacity and hypertension, 245
injuries, non-penetrating, 270
lanatoside C, effect of, 337
leptazol, effect of, 337
mural thrombi, 218
nicotine, effect of, 409
non-penetrating traumatic injuries, 270
recruit's, 2
rheumatic disease, 252
recovery of haemolytic streptococci, 377
two-step, test, 378

- Heart—continued**
 right, hypertrophy, 252, 291
 situs inversus, complete, with visceral pain, 246
 soldier's, 2
 sounds, recording of, 245
 transposition of great vessels, 248
 valvular disease, 252
 wounds of, 249
- Heart-block**
 Adams-Stokes attack and the electrocardiogram, 246
 bundle-branch, relation to cardiac enlargement, 150
- Heart failure, 253**
 congestive, prognosis of, 253
 following administration of desoxycorticosterone, 132
 treatment, 253
 calcium gluconate, 254
 medical therapy and general management, 253
 mercurial diuretics, 253
 ouabaine and digitalis, 254
 vitamin B₁, 254
- Heat**
 effect on shock, 387
 reduction by drugs, 339
 rheumatism treated with, 229
- Heberden's nodes, 243**
- Helium and oxygen in treatment of asphyxiated infants, 156**
- Helium-oxygen**
 inhalation in treatment of laryngitis, 281
 mixture, effect on voice, 335
 therapy, aero-otitis media, in, 182
- Hellebore, green. See Veratrum viride**
- Hemiplegia, post-operative, associated with hypotension, 167**
- Heparin, 12**
 cavernous sinus thrombophlebitis treated by, 408
 prevention of blood clotting, 335
 pulmonary embolism treated by, 296
 retinal venous thrombosis treated with, 376
 subacute bacterial endocarditis treated by, 251
 sulphapyridine and, 251
 thrombophlebitis treated by, 296, 297
 use in prevention of post-operative thrombosis, 335
 use in surgery and thrombosis, 335
- Hepatectomy, partial, effects of colchicine after, 334**
- Hepatic cirrhosis. See Liver, cirrhosis**
- Hepatitis**
 acute,
 operation for appendicitis, after, 149
 chronic,
 abdominal venous thrill, 288
 alcoholism and, 135
 predominant jaundice, with, 289
- Hepato-lienal fibrosis, 398**
- Hepato-splenomegaly-lipoidosis, of Bürger and Grutz, 287**
- Hepato-trophic properties of sex hormones, 381**
- Hepatosiis, pre-cirrhotic, in alcoholism, 135**
- Hereditary**
 ectodermal dysplasia, 147
 haemorrhagic disorders, 241
 oedema, 318
 telangiectasia with visceral involvement, 232
- Heredity**
 constitution, and, 254
 tumours in twins, 254
- Hernia, 255**
 amniotic, 255
 eventration, 255
 external abdominal, 255
 hepatic disease and ascites associated with, 255
 inguinal,
 cord transplantation in, 255
 new operative technique for, 255
 injection treatment, end results of, 255
 treatment of, 14
 umbilical cord, in, 255
- Herpes, 255**
 labialis, treated with spiritus vini rectificatus, 256
 simplex,
 associated with arsenical dermatitis, 256
 treatment, moccasin snake venom, 256
 zoster,
 aberrant vesicles, 256
 aetiology, 255
 association with chicken-pox, 255
 clinical picture, 256
 mumps complicated by, 309
 ophthalmicus, convalescent blood in treatment, 198
 paralysis following, 256
 treatment, 256
 anaesthetic infiltration, 256
 X-ray of the spine, 256
- Hexamine, tetanus treated by, 407**
- Hexazole, 79. See also Cardiazol**
- Hexobarbitone soluble. See Evipan soluble**
 basal hypnotic, as, 142
 blood-oxygen capacity after, 142
- Hexylresorcinol, trichomonas vaginalis treated by, 429**
- Hibernation, cancer treated by, 184**
- High-frequency currents, effect on the body, 217**
- Hippuric acid, excretion, in hyperthyroidism, 236**
- Hirsuties, adrenal hypertrophy causing, 243**
- Histaminase**
 skin tests in allergic cases, 136
 treatment of allergic dermatoses, in, 137
- Histamine**
 effect of vitamin C on muscle response to, 425
 like substance in shock, 386
 Ménière's syndrome treated with, 422
 peptic ulcer, relation to, 326
 phosphate, injections, effect on pressure of cerebrospinal fluid, 188
 rôle in allergic reactions, 136
 shock, rôle in, 386
- Histoplasma capsulatum, 257**
- Histoplasmosis, 257**
 clinical picture, 257
 occurrence in infant, 257
- Hodgkin's disease, 257**
 abdominal, 258

INDEX

- Hodgkin's disease—*continued*
 brucella infection associated with, 257
 diagnosis and differential diagnosis, 258
 Gordon reaction, reliability of, 258
 haemoptysis in, 258
 intrathoracic, 258
 respiratory tract, 258
 urinary bladder, in, 258
- Homosexuality, leptazol therapy, 385
- Hormodendrum pedrosoi*, 233
- Hormone therapy
 eunuchism and hypogonadism, 384, 385
 involutinal melancholia, 365
 menopausal disorders, in, 190, 191
 menstrual and climacteric disorders, 384
 mental disorders, in, 81
 obesity in children, 130
 undescended testis, 5, 406
 vaginitis, 429
- Hormones, 335. *See also under names of the various hormones*
 androgens, 384
 anterior pituitary, 382
 desoxycorticosterone, 383
 desoxycorticosterone acetate, 335
 endometrial extract, 383
 gonadotrophic, rôle in psychiatry, 364
 ketosteroids, neutral, rate of excretion of, 384
 male sex hormone, clinical uses of, 384
 oestradiol, 335, 382
 oestrogens, 382, 383. *See Oestrogens*
 ovarian and synthetic oestrogenic substances, 382
 ovarian follicle-stimulating, 382
 perandren, 382
 pitressin, 336
 pituitary, 351
 gonadotrophic extracts, 336
 pregnancy, 357
 pregnanediol. *See Pregnanediol*
 progesterone, 384
 progynon, 382
 sex, 381
 blood pressure, relation to, 382
 carcinogenic action of, 183
 effect on cancer tissue, 183
 effect on liver and heart, 381
 effect on ovary, 22
 effect on uterine bleeding, 21
 excretion in children, 382
 hepato-trophic and cardio-trophic properties of, 381
 male, 384
 malignant disease treated by, 184
 rôle in psychiatry, 364
 treatment of menstrual and climacteric disorders, 384
 stilboestrol, 383
 testosterone, 382, 384, 385
 thyroïdotrophic, 382
- Hospital equipment, disinfection of, and control of infection, 185
- Hospitals
 control of dust in, 185
 irradiation of air in, 130
- Hutchinson's teeth in non-syphilitics, 202
- Hydatid cyst
 bone, of, 259
 ilium, of, 259
- Hydatid cyst—*continued*
 kidney, of, surgical treatment, 258
 uterus, of, 419
- Hydatid disease, 258
- Hydatidiform mole, 190
- Hydrargyria
 maligna, 224
 mitis, 224
 simplex, 224
- Hydrocarbons, chlorinated, poisoning by, 411
- Hydrocele
 canal of Nuck, of, 330
 injection treatment, final results of, 406
- Hydrocephalus, unilateral internal, 259
- Hydrochloric acid and collargol test, 188
- Hydrogen sulphide, poisoning during permanent wave, 410
- Hydrometrocolpos in infants, 430
- Hydroxylthylapocupreine, pneumonia treated by, 354
- Hyoscine, use in convulsion therapy, 79
- Hyperaesthesia, cutaneous abdominal, in dyspeptics, 215
- Hyperchlorhydria
 aetiology, 259
 fruit juice, effect of, 259
- Hyperemesis
 gravidarum, aetiology of, 358
 hiemis, 232
- Hyperkeratosis, palms and soles, of, 191
- Hypernephroma, 277
 metastases simulating aneurysms, 133
 renal, and virilism, 133
- Hyperparathyroidism, 322
 clinical features, 322
 clinical types, 322
 dental symptoms, 322
 morbid anatomy, 323
 mouth, condition of, 322
 renal calcification in, 144
 renal insufficiency complicating, 323
 spinal osteoporotic type, 322
- Hypertension
 body build, relation to, 166
 electrocardiogram in, 245
 essential,
 aetiology, 165
 childhood, in, 164
 degrees of fluctuation in, 165
 supradiaphragmatic splanchnectomy, 164
 functional capacity of heart and, 245
 influence of doctor on hypertensive patients, 164
 malignant, 164
 migraine and headaches, relation to, 306
 nephritis, relation to, 312
 nephrotic syndrome with, in diabetes mellitus, 205
 renal disease associated with, 165
 chemotherapy, 165
 metabolic activity of kidneys, 165
 pyelonephritis, 165
 treatment with depressor renal extract, 166
 renal ischaemia and, 2, 3
 toxæmias of pregnancy, and, 18

INDEX

- Hyperthyroidism
 associated with menopause, 190
 excretion of hippuric acid in, 236
 Hypertrichosis, female, in, adrenal hypertrophy causing, 243
 Hyperventilation, aviation, in, 159
 Hypnosis, evipan, in investigation of neuroses, 259
 Hypnotism, 259
 Hypochlorite, electrolytic, in treatment of burns, 180
 Hypochromic deficiency anaemias, 139
 Hypodermic syringes, transmission of malaria by, 301
 Hypoglycaemia
 atrophy of adrenals and, 260
 spontaneous, 260
 spontaneous, in Simmonds's syndrome, 390
 Hypogonadism, treatment by testosterone and testosterone propionate, 384
 Hypoparathyroidism, 322
 pregnancy, in, 323
 Hypoproteinaemia, vitamin K therapy, 427
 Hypotension
 incidence and aetiology, 167
 post-operative hemiplegia associated with, 167
 postural, 166, 167
 systolic and diastolic pressures, 167
 Hypothyroidism, carbohydrate tolerance in, 306
 Hypovitaminosis. *See* Deficiency diseases; Vitamins
 Hysterical paralysis, soldier, in, 363
- I
- Icterus gravis neonatorum, 140, 141
 erythroblastosis with, 140
 hepatic changes in, 141
 vitamin K therapy, 141
 Idiopathic steatorrhoea, 26
 Ileitis, regional. *See* Crohn's disease
 Ileus
 gall-stone, 125
 paralytic, use of Miller-Abbott tube in, 272
 Ilium, hydatid cyst involving, 259
 Immunity, 260
 acquired, 260
 active, effect of ultra-violet irradiation, 260
 passive, 260
 practical applications, 260
 streptococcal infections, 261
 Immunization, 260
 combined, in tetanus and diphtheria, 260
 enteric fevers, 261
 infectious diseases, 69
 scarlet fever, 378
 tetanus and enteric fever, 407
 typhus fever, epidemic, 416
 Impetigo, treatment, 120
 Impotence, treatment by testosterone propionate, 261
 Infancy
 broncho-pneumonia in, 178
 diarrhoea in, 208
 Infant feeding, 262
 dextrin-maltose-dextrose carbohydrate, use of, 262
 relation of maternal diet to lactation, 262
 vitamins in, 49
 Infantile
 arteriosclerosis, 152
 scurvy, 379
 Infants
 histoplasmosis in, 257
 oestradiol and desoxycorticosterone acetate for, 335
 plasma-prothrombin titrations in, 241
 pneumonia in, 352
 scurvy in, 379
 Infarct
 cardiac, 249
 rupture of interventricular septum due to, 146
 pulmonary. *See* Lung, infarction
 Infections
 acute, 62
 air-borne, diphtheria, 209
 carbohydrate metabolism and, 306
 cross, 13
 irradiation of air in hospitals, 130
 wounds of. *See* Wounds, infected
 Infectious diseases, 4, 62
 immunization scheme, 69
 Influenza, 262
 bronchiolitis, acute, in, 263
 buccal spots in, 263
 clinical picture, 263
 epidemiology, 262
 virus strains, variation of, 262
 viruses of, 3
 war-time, in, 263
 Inguinal adenitis, lymphopathia venereum causing, 300
 Injection treatment
 haemorrhoids, 375
 hernia, of, 255
 hydrocele, of, 406
 Injections, pharmacopoeial, 112
 Injuries, 263. *See also* Wounds
 crush, 269
 Inquests, fees at, 199
 Insulin. *See also* Diabetes mellitus
 pulmonary tuberculosis treated by, 293
 shock therapy, 81
 compression fracture of spine, 367
 economical war-time method, 367
 effect on cerebrospinal fluid proteins, 368
 intravenous administration, 368
 schizophrenia, in, 367, 368
 Insulin, zinc protamine, 206
 Insulin-quinine mixture, diabetes mellitus treated with, 207
 Interauricular septum, defects of, 247
 Inter-capillary glomerulo-sclerosis and diabetes mellitus, 152
 Inter-menstrual pain, 21
 Interventricular septum. *See* Septum
 Intervertebral disks
 dislocation of, 14
 protruded, associated with osteitis deformans, 396
 Intestinal obstruction, 271
 acute, 271

INDEX

Intestinal obstruction—*continued*

- acute—*continued*
 - clinical picture, 271
 - diagnosis, 271
 - gall-stones or endoliths causing, 125
 - radiological examination, 271
 - reversed rotation of intestine accompanied by encapsulating peritonitis, 271
 - treatment, 272
 - intraperitoneal sulphanilamide, 272
 - Miller-Abbott tube, 272
 - adhesions causing, 330
 - congenital bands causing, 272
 - small intestine, 272
- Intestine
- gas cysts of, 272
 - intubation, in treatment of intestinal obstruction, 272
 - reversed rotation of, 271
 - simple ulcers of, 193
 - small,
 - effect of X-ray therapy on, 372
 - giardial infection, 24
 - obstruction of, 272. *See also* Intestinal obstruction
 - congenital bands, by, 272
 - tuberculosis, 273
- Intracranial
- syphilis, 315
 - volume, effect of altitude changes on, 160
- Intramuscular lipoma, 310
- Intra-ocular pressure, high altitudes, at, 160
- Intrasternal introduction of bone marrow, 141
- Intravenous therapy
- bacterial and protein contamination, 337
 - pyrexial reactions, 337
- Intussusception, chronic, clinical picture, 126
- Involucional melancholia
- convulsion therapy, 79
 - endocrine therapy in, 191, 365
- Iodized oil. *See* Lipiodol
- Iodobismittel, neurosyphilis treated by, 316
- Ionization, pelvic iontophoresis, 217
- Iontophoresis, pelvic, 217
- Irido-cyclitis
- tuberculous, 420
 - ureo-parotitis, 420
- Iritis, ankylosing spondylitis, in, 156
- Iroko wood, dermatitis caused by, 203
- Iron, deficiency, essential juvenile, 139
- Irradiation
- air in hospitals, 130
 - necrosis following, 130
- Isinglass, transfusions of, in haemorrhage, 269
- Itch, cat, 390
- Ivy, poison, dermatitis caused by, 203

J

- Jaundice, 273
- acholuric, differential diagnosis, 141
 - after operation for appendicitis, 149
 - arsphenamine causing, 332
 - familial non-haemolytic, 141
 - hepatitis, chronic, with predominant, 289
 - non-haemolytic, familial, 141

E.M.S. II

Jaundice—*continued*

- nuclear, 141
 - obstructive hepatic, 273
 - hypovitaminosis A and D, 273
 - post-operative vitamin K deficiency, 273
 - pre-operative administration of vitamin K, 273
 - prolonged dark-adaptation in, 273
 - prothrombin deficiency in, 273
- Jaws
- estimation of age from, 303
 - ulcer, non-malignant, 308
- Jejunocolic fistula, nutritional oedema due to, 318
- Jejuno-ideal insufficiency, chronic, 26
- Jejunum
- leiomyo-sarcoma of, 272
 - primary carcinoma of, 272
 - sarcoma of, 272
 - sprue, in, 27
- Jensen's rat sarcoma, X-ray therapy, 372
- Joints
- diseases and disorders, 274
 - sprains, procaine injections for, 159
 - tuberculosis, 274
- K
- Kahn test, 103
- Kala-azar
- diamidines in, 100
 - treatment by 4 : 4'-diamidinostilbene, 274
- Keloid, aetiology of, 275
- Keratitis, intravenous injections of ascorbic acid in, 198
- Keratodermia, senile, 191
- Keratomalacia, vitamin A deficiency and, 209
- Keratosis, 394
- follicularis, vitamin A therapy in, 200
- Kernikterus, icterus gravis neonatorum, in, 141
- Ketosteroids, neutral, rate of excretion of, 384
- Kettering hypertherm, general paresis treated by, 105
- Kidney
- calcification, dissecting aneurysm secondary to, 144
 - calcium plaques in, 312
 - calculus. *See* Calculus, renal
 - complications due to sulphathiazole, 343
 - congenital abnormalities, 275
 - disease, hypertension and, 165
 - extracts in treatment of renal hypertension, 166
 - fusion, 275
 - hydatid cyst, surgical treatment of, 258
 - hypernephroma, 277
 - metastases simulating aneurysms, 133
 - virilism, and, 133
 - impairment of function in crush injuries, 269
 - injuries, 276
 - insufficiency,
 - blood transfusion causing, 170
 - prolonged, complicating hyperparathyroidism, 323
 - ischaemia of, and hypertension, 2, 3
 - lupus erythematosus, in, 299
 - malignant disease, metastatic, 277

2 G

INDEX

Kidney—continued

- nephrotic syndrome with hypertension in diabetes mellitus, 205
 - polycystic disease, death from acute uraemia, 275
 - post-operative damage, 276
 - radiography, 372
 - sclerosis, pregnancy toxaeias and, 357
 - surgical diseases, 275
 - tumours, 277
 - diagnosis, 277
 - fever as initial symptom, 277
 - metastatic, 277
- ## Knee
- granuloma, traumatic, 274
 - synovial membrane, glomus tumour of, 393
 - synovium, malignant, 274
- ## Korsakow's syndrome, 369

L

Labour, 278

- anaesthesia and analgesia, 280
 - evipan soluble, 280
 - paraldehyde analgesia with perineal anaesthesia, 280
- course of, 278
- delayed, 279
- effect of bombing on, 19
- evisceration and embryotomy, 279
- factors in, 278
- failure of dilatation of os, 279
- induction of, 279
 - alkalinizative and pituitary extract, 279
 - high puncture of membranes, 279
 - posterior pituitary extract, 16, 279
 - uroselectan B, by, 19
- normal, 278
- obstructed,
 - evisceration and embryotomy, 279
 - failure of dilatation of os, 279
 - foetal ascites causing, 279
- obstructions in cervix, 279
- onset, oxytocic substance and pituitrin, 278
- operative and manipulative procedures, 279
- pains, relief of, by raspberry leaves, 20
- prolapse of cord, 278
- radiology, 280
- sedatives in, 280
- vitamin K therapy in, 428
- X-ray examination in, 280
 - placental implantations, 280
 - soft tissue radiography, 280
 - visualization of placenta, 280

Lacrimal

- apparatus, diseases, 281
- glands,
 - Boeck's sarcoid of, 281
 - tumours, 281

Lactation

- cystine, glycine, and glutamic acid, effect of, 262
- excretion of mandelic acid, 262
- inhibition by stilboestrol, 262
- oestrogens, effect of, 383
- relation of maternal diet to, 262

Lactal obstruction, sprue syndrome, and, 28

Lambia intestinalis, 24. *See Giardia intestinalis*

Lamblia, 24. *See Giardiasis*

Lanatoside C, effect on heart, 337

Larva migrans, treatment, 310

Laryngeal neuralgia, superior, 314

Laryngitis, acute, helium-oxygen inhalation in, 281

Laryngocele, pseudo-, 311

Laryngology, 52

Laryngo-tracheobronchitis, chemotherapy in, 281

Larynx

- Boeck's sarcoidosis, 281
- diseases, 281
- malignant growths, anaesthesia for, 282
- tumours, 281

Lateral sclerosis, amyotrophic, vitamin E therapy, 307

Laurence-Moon-Biedl syndrome

'forme fruste', 351

incomplete form of, 162

without polydactyly and mental deficiency, 351

Lead

- poisoning, 282
 - aetiology, 282
 - bullets lodged in tissues causing, 282
 - central nervous system in, 282
 - clinical picture, 282
 - diagnosis, 282
 - encephalopathy in children, 282
 - encephalopathy simulating cerebral tumour, 282
 - printers, in, 282
 - renal calculus containing, 276

Lederer's anaemia, 140

Legs

- bilateral oedema of, 318
- oedema of, persistent, 318

Leiomyosarcoma

- inferior vena cava, of, 422
- jejunum, of, 272

Lenses, lacquered, use in strabismus, 402

Lenticular nucleus, functions of, 90

Leprosy, 283

geographical incidence, 283

Great Britain, in, 283

mixed types, 283

pathology and bacteriology, 283

treatment, 283

basic principles, 283

blood transfusion, 283

diphtheria formol toxoid, 284

Grasset's tubercle endotoxoid, 284

tuberculoid, 283

ulceration in, 284

Leptazol, 79. *See also* Cardiazol

cardiographic changes due to, 337

psychomotor efficiency, effect on, 337

shock therapy,

bilateral fracture of femoral neck caused by, 366

cardiovascular patients, in, 367

effect on cerebrospinal fluid proteins, 368

fractures of spine caused by, 366

memory defects following, 367

results of, 367

therapy,

affective psychoses, in, 365

compulsion neurosis, in, 364

INDEX

Leptazol—*continued*
 therapy—*continued*
 homosexuality and lesbianism, 385
 sub-convulsant doses, 365
 Lesbianism, leptazol therapy, 385
 Leucocytes, supravital staining of, 7
 Leucoplakia, 394
 vulva, of, mercury sulphide tattoo for, 430
 Leucorrhoea, monilial vaginitis and, 284
 Leucotomy
 frontal,
 technique, 82
 treatment of mental disorders, in, 81, 82
 Leukaemia, 285
 aleukaemic myeloid, subacute, 286
 chronic myeloid, 285
 leukaemoid reactions and, 285
 lymphocytic, treatment by sulphapyridine, 286
 monocytic, acute, 286
 myelocytic, 285
 chloroma and, 285
 chronic, 285
 clinical picture, 285
 leukaemoid reactions and, 285
 myeloid, subacute aleukaemic, 286
 skeletal symptoms in, 286
 subacute aleukaemic myeloid, 286
 treatment, X-rays, 'spray' technique, 285
 Leukaemoid reactions, 285
 Lice, 391
 Lichen
 planus, 286
 aetiology, 286
 involving nail-bed, 287
 treatment by vitamin B, 287
 Light sense apparatus, Livingston's, 31
 Limbal tumours, 196
 Limbs, prolonged compression of, 269
 Lipid pneumonia, 177
 Lipiodol
 myelography, in, 371
 radiography of maxillary antrum, 127
 Lipocaiac, erythraemia treated by, 225
 Lipoid granulomatosis. *See* Schüller-Christian syndrome
 Lipoidoses, 287
 differential diagnosis, 287
 Gaucher's disease, 287
 Schüller-Christian syndrome, 287
 xanthomatous biliary cirrhosis, 287
 Lipoma
 intramuscular, 310
 soleus muscle, in, 310
 Lips
 herpes, treated with spiritus vini rectificatus, 256
 irritation due to lip-stick, 203
 Lip-stick cheilitis, 203
 Liquid paraffin, disinfection of hospital equipment by, 185
 Listerella organisms, glandular fever, relation to, 235
 Little's disease, treatment by β -erythroidine hydrochloride, 332
 Liver
 carcinoma, primary, 289
 circulation of blood in, 288
 cirrhosis,
 abdominal venous thrill, 288

Liver—*continued*
 cirrhosis—*continued*
 ascites, and, associated with hernia, 255
 Hanot's unilobular, 289
 multiple neuritis, relation to, 289
 pre-cirrhotic hepatosis in alcoholism, 135
 diseases of, 288
 effect of sex hormones on, 381
 function tests, 4, 288
 comparative review, 288
 intrahepatic circulation of blood, 288
 phenolphthalein, 288
 quartz-rod transillumination, 288
 histopathological changes in burns, 178
 necrosis, sulphanimide as possible cause, 343
 partial removal, effects of colchicine after, 334
 phenolphthalein, effect of, 288
 rupture, with subsequent 'sequestrum', 263
 stilboestrol, alleged toxic action of, 383
 tumours, 289
 morbid anatomy, 289
 racial incidence, 289
 Livido reticularis, 224
 Livingston's
 angular depth perception apparatus, 31
 light sense apparatus, 31
 rotating stereogram, 31
 Lobotomy, pre-frontal, in treatment of mental disease, 365
 Löffler's syndrome, 157
 Longevity, sex and profession as factors, 379
 Looser's zones, 171
 Louse, 391
 Low-voltage varying currents, used for shock-therapy in mental disease, 218
 Lumbago, 161
 Lung
 abscess, 290
 acute putrid, 76
 classification, 290
 pathology and morbid anatomy, 290
 treatment, 290
 bronchoscopic, 290
 sulphapyridine, 290
 blast injuries, 297
 clinical picture, 297
 effect on lungs, 297
 experimental investigation, 298
 phrenico-costal sinus pneumonia, 298
 results of air-raids, 297
 carcinoma, 294
 cardiac metastases, 294
 primary, 294
 'sulcus tumour', 294
 diseases, 71, 290
 fibrosis,
 diagnosis of, 294
 scleroderma and, in Raynaud's phenomenon, 375
 infarction, pneumothorax due to, 290
 oedema of, associated with menstruation, 318
 post-operative complications, 295
 extension of tuberculosis, 292
 pulmonary embolism, 295
 diagnosis, 296

INDEX

- Lung—*continued*
 post-operative complications—*continued*
 pulmonary embolism—*continued*
 heparin therapy, 296
 incidence and occurrence, 295, 296
 multiple chest - lead cardiograms, 296
 operative prevention, 296
 predisposing conditions, 295
 thrombophlebitis and, 296
 treatment, 296
 'sulcus tumour' of, 294
 tumours, 294
 malignant, 294
 non-malignant, 294, 295
 Lupus erythematosus, 299
 atypical verrucous endocarditis combined with, 250
 clinical types, 299
 renal involvement, 299
 systemic, compared with dermatomyositis, 309
 treatment by sulphonamides, 118, 299
 Lupus vulgaris, 299
 treatment by Grasset's tubercle endotoxoid, 300
 Lygranum, 109
 Lymphatic glands,
 diseases, 300
 fat, in, 300
 inflamed areas, in, 300
 Lymphogranuloma inguinale, 109
 diagnosis, 109
 ocular, 109
 treatment, 109
 Lymphopathia venereum, 300
 clinical picture, 300
 conjunctivitis, chronic unilateral, due to virus of, 300
 infection of alimentary tract, 300
 inguinal adenitis due to, 300
 swallowing of virus in, 300
 treatment by sulphonamides, 300
 ulcerative colitis, relation to, 193
 Lymphosarcoma, treatment of, 300
- M
- M & B 693, *corynebacterium diphtheriae*, action on, 341
 Magnesium
 sulphate, acute nephritis treated by, 312
 trisilicate, peptic ulcer treated by, 328
 Magnetotherapy, 217
 Malaria, 96, 301
 aetiology, 301
 control of, 98
 diagnosis, 301
 epidemiology in war areas, 96
 parasites, rapid staining technique, 301
 prophylaxis, 97
 therapy,
 control of undesirable symptoms, 301
 effect of sulphathiazole on rigors, 301
 general paralysis of insane, in, 315
 thio-bismol controlling, 301
 transmission,
 blood transfusions, by, 97
 hypodermic syringes, by, 301
 Malaria—*continued*
 transmission—*continued*
 stored blood, in, 301
 treatment, 98
 Malignancy
 diagnosis by biochemical methods, 183
 sedimentation of red cells in, 163
 Malignant disease. *See* Cancer
 Mandelic acid, 112
 excretion in breast milk, 262
 Mantoux test, and tuberculin patch test, 292
 Mapharside
 after recovery from arsphenamine dermatitis, 332
 syphilis treated by, 404
 Marble bones, 171
 March fracture, bilateral, 211
 Marchiafava-Micheli syndrome, 140
 Mare's serum, male sterility treated by pregnant, 400
 Mass radiography, 75, 76
 Mastitis, chronic, testosterone inunction in, 175
 Measles, 302
 complications, 302
 diagnosis, 68
 encephalitis and paraplegia complicating, 302
 placental extract and convalescent serum in, 302
 prophylaxis, 68, 302
 purpura complicating, 302
 treatment, 68
 Mecholyl. *See* Acetyl- β -methylcholine bromide
 Mediastinal flutter, 302
 Mediastinum
 diseases, 302
 ganglioneuroma, 303
 traumatic lesions, 302
 tuberculosis, 302
 tumours, 303
 Medicine, advances in, 1
 Medico-legal examinations and reports, estimation of age from teeth and jaws, 303
 Megacolon, treatment by acetyl- β -methylcholine bromide, 303
 Meinicke flocculation test, tuberculosis, in, 414
 Melancholia
 involutional,
 convulsion therapy, 79
 endocrine therapy, 365
 treatment, 191
 Melano-carcinoma of adrenal gland, 133
 Melanoma, malignant, of conjunctiva, 196
 Membranes, foetal, high puncture of, 279
 Memory, defects following leptazol therapy, 367
 Menaphthone, 113
 Ménière's syndrome, treated with histamine, 422
 Meningitis
 chemotherapy in, 58
 diagnosis from tularaemia, 415
 influenzal, treated by sulphapyridine, 305
 otogenous, 217
 pneumococcal, treatment by sulphonamides and antiserum, 304

INDEX

- Meningitis—*continued*
 pyogenic, treatment by sulphapyridine, 304, 305
streptococcus viridans causing, treated by sulphapyridine, 304, 305
- Meningocele, cranioleucunia associated with, 396
- Meningococcal
 endocarditis, without meningitis, 250
 septicaemia, 4
 purpura and adrenal haemorrhage associated with, 186
- Meningococcus, adrenal haemorrhage caused by, 132
- Menopause. *See* Climacteric
- Menstruation
 blood electrolytes and, 163
 disorders, sex hormone therapy, 384
 intermenstrual pain, 21
 oedema of lung associated with, 318
 oestrogens and, 21
 testosterone propionate and, 21
- Mental
 disease, 79
 treatment, electric shock, 218
 war, influence of, 363
- disorders,
 biochemical mechanisms, 84
 convulsion therapy, 79
 electrical convulsions in treatment, 80
 frontal leucotomy, 81, 82
 hormone therapy, 81
 insulin shock therapy, 81
 nitrogen balance in, 84
 organic, 84
 sex hormones, rôle of, 364
 surgical therapy, 81, 82
- symptoms,
 narcolepsy, in, 311
 neurosyphilis, in, 316
- Mercurial diuretics, in treatment of heart failure, 253
- Mercury
 ointment, ammoniated, idiosyncrasy in children, 332
 organic compounds, poisoning by, 411
 sulphide, tattoo for leucoplakia vulvae, 430
 syphilis treated by, 404
- Mesenteric
 thrombosis and embolism, 125
 vascular occlusion, 125
- Metabolism, 305
 basal, hypothyroidism and hyperthyroidism, in, 306
 carbohydrate, and infection, 306
 Crohn's disease, in, 200
 disordered,
 dermato-myositis, in, 309
 psoriasis, in, 362
 serum proteins, 305
- Metastases
 kidney, in, 277
 ureteral, 278
- Metatarsal bone, supernumerary, 232
- Methaemalbumin, 7, 170
- Methaemoglobin, 7
- Methyl
 chloride, poisoning by, 411
 mercury compounds, poisoning by, 411
 testosterone, eunuchism treated by, 385
- Metrazol. *See* Cardiazol
- Meulengracht régime, peptic ulcer treated by, 328
- Micrococcus albicans*, black hairy tongue caused by, 308
- Middle ear
 Schüller-Christian syndrome involving, 287
 suppuration, extra-dural abscess caused by, 216
- Migraine, 90, 306
 aetiology, 306
 diagnosis, 307
 headache of, 91
 hypertension, relation to, 306
 neuralgia, migrainous, 307
 treatment by oxygen inhalation, 307
- Migrainous neuralgia, alcohol treatment, 307
- Milk
 gastro-intestinal allergy due to, 138
 human, excretion of mandelic acid in, 262
 spore-forming bacteria in, 232
- Miller-Abbott tube, in treatment of intestinal obstruction, 272
- Mineral oil, laxatives and vitamin A deficiency, 426
- Miners
 of bituminous coal, silicosis in, 389
 vitamin A requirements of, 426
- Mitosis, effect of irradiation on, 416
- Mitral stenosis
 ball thrombi, 252
 rheumatic, 252
 signs of early, 44
- Mixed tumours, parotid gland, of, 323
- Moccasin snake venom, herpes simplex treated by, 256
- Mole, hydatidiform, 190
- Monilia, in vaginitis, 284
- Monilia albicans*, 285
- Monoethanolamine oleate, sensitivity to, 421
- Monolate, sensitivity to, 421
- Mononucleosis, infections. *See* Glandular fever
- Monorchia, 231
- Morphine
 addiction, treatment by refrigeration, 350
 relief of pain by prostigmin methylsulphate and, 338
- Motor neurone disease, 307
- Mouth
 carcinoma, tobacco chewing and, 308
 condition of, in hyperparathyroidism, 322
 diseases, 307
 infections of, chemotherapy in, 60
 'sore' and vitamin B₁₂, 308
- Mucinous carcinoma of breast, 176
- Mucous membrane
 gastric, presence of spirochaetes in, 401
 nasal, anti-poliomyelitic substances from, 356
- Mule-spinner's cancer, 392
- Multinucleosis among Bantus, 416
- Mumps
 nervous system in, 309
 polyradiculitis, myelitis and herpes zoster complicating, 309
- Mural thrombi, as source of emboli, 218
- Murmur, functional, 45

INDEX

- Muscles
diseases, 309
 vitamin E therapy, 230, 426
dystrophy. *See* Muscular dystrophy
fibrillation, peripheral origin of, 229
lipoma, 310
response to histamine, effect of vitamin C on, 425
tension, 84
tumours, 310
- Muscular
dystrophy, 310
 vitamin B₆ therapy, 428
 vitamin E therapy, 5, 50, 426, 428
fatigue, amino-acetic acid and gelatin, effect of, 331
- Muscularis mucosal, paralysis of, and sprue syndrome, 27
- Myalgia, idiopathic, 229
- Myalgic spots, 229
- Mycobacterium*
 leprae, 284
 tuberculosis, 284
- Myelitis, mumps complicated by, 309
- Myelography, iodized oil, with, 371
- Myeloid sarcoma, 172
- Myeloma
 multiple, of bone, 173
 solitary, of bone, 173
- Myiasis, 310
- Myocardial infarction, rupture of interventricular septum due to, 146
- Myocarditis, 249
 acute interstitial, arsphenamine causing, 332
- Myocardium
 diseases, 249
 infection, pain in shoulder as sequel, 249
- Myopia, sulphonamide therapy causing, 310
- Myositis, 309
- Myotonia, vitamin E therapy, 426
- N
- Nail polish, dermatitis caused by, 203
- Nails
 absence of, with bony changes, 230
 diseases of, 311
 dystrophies, 311
 glomus tumour, 311
 lichen planus of nail-bed, 287
 longitudinal striation, 311
 new growth, 311
 psoriasis, X-ray therapy for, 362
 transverse lines, 311
- Naphthalene, exfoliative dermatitis due to, 204
- Narcolepsy, mental symptoms, 311
- Narcosis, basal, 142
- Nasal
 mucosa, antiseptic snuffs, action of, 331
 sepsis, acriflavine and proflavine in prevention of, 330
 septum, dermoid cyst of, congenital, 204
 sinuses, accessory. *See* Sinuses, nasal accessory
- Nasopharynx
 diseases, 317
 juvenile basal fibroma of, 317
 tumours, 317
- National war formulary, 112
- Neck
 cysts, 311
 tumours, 311
- Necrobiosis lipoidica diabetorum, 395
- Necrosis, post-irradiation, 130
- Nematodes, 311
- Neoarsphenamine
 neurosyphilis treated by, 316
 staphylococcal infection treated by, 342
 urethritis treated by, 417
- Neocryl
 neurosyphilis treated by, 317
 toxicity of, 317
- Neokharsivan, anthrax, in treatment of, 147
- Neo-prontosil, reduction in tissue suspensions, 343
- Neosynephrin, maintaining blood pressure during spinal anaesthesia, for, 142
- Nephrectomy, effect on pressor response to renin, 166
- Nephritis, 312
 chronic, vicious circle in, 312
 clinical picture, 313
 course and prognosis, 313
 glomerulo. *See* Glomerulo-nephritis
 hypertension and, 312
 morbid anatomy, 312
 scarlet fever, in, 313
 treatment, 313
- Nephrosclerosis, pregnancy toxæmias and, 357
- Nephrosis, 312
 treatment, 313
 acacia, 314
 vitamin A, 313
- Nephrotic syndrome with hypertension in diabetes mellitus, 205
- Nephro-ureterectomy, for primary carcinoma of ureter, 277
- Nerve
 eighth, affections of, 199
 grafts, 95
 suture, use of coagulated blood plasma in, 264
- Nerves
 peripheral,
 anatomy of, 88, 89
 grafting, 95
 pellagra, in, 324
 plasma-fibrinogen technique in repair of, 94
 repair of lesions, 94
- Nervous
 diseases, 88
 vitamin E therapy, 426
 factors, shock, in, 386
 symptoms,
 bacterial endocarditis, in, 250
 chicken-pox, in, 189
 diabetes mellitus, in, 206
 extraction of teeth, after, 202
 mumps, in, 309
 system
 central, in lead poisoning, 282
 opiates, effects of, 338
- Neuralgia, 314
 atypical, 314
 buccal, 314
 migrainous, alcohol treatment of, 307

INDEX

- Neuralgia—*continued*
 superior laryngeal, symptoms and diagnosis, 314
 trigeminal, vitamin B₁ therapy, 314
- Neuritis
 multiple, 315
 acute infective, 315
 arsenical, vitamin B therapy in, 410
 associated with diabetes mellitus, 206
 Guillain-Barré syndrome, 315
 haematoporphyrinuria acuta complicated by, 239
 hepatic cirrhosis, relation to, 289
 peripheral. *See* multiple, *supra*
- Neurocirculatory asthenia, 2
- Neurofibroma, acoustic, 174
- Neurology, 88
- Neuroses. *See* Psychoneuroses
- Neurosyphilis, 315
 conjugal, 403
 mental disturbances in, 316
 prophylaxis, 316
 treatment, 315, 316
 iodobismutol and saligenin with neoarsphenamine or tryparsamide, 316
 tryparsamide and neocryl, 317
- New-born
 asphyxia in, 156
 atelectasis, massive, in, 290
 dacryocystitis, treatment of, 281
 eventration in, 255
 haemolytic anaemias of, 140
 haemorrhagic disease of,
 vitamin K in treatment, 50, 427
 icterus gravis neonatorum, 140, 141
 prothrombin time, effect of vitamin K on, 427
- Nicotine
 effect on normal and damaged hearts, 409
 fatal poisoning in child, 409
 gastric acidity, effect on, 326
- Nicotinic acid, 112, 121
 senile toxic exhaustion syndromes treated by, 82
 sprue treated by, 399
 therapy, pellagra, 324
 xerostomia due to deficiency, 424
- Night
 blindness, 5
 flying, 30, 31
 vision, of aviators, 36
 visual capacity of aviators, 30, 31
- Nikethamide, 112
- Nipples, discharge from, 176
- Nitrogen
 metabolism, in mental disorders, 84
 monoxide and oxygen, anaesthesia for operations on malignant growths of larynx, 282
- Nitrogenous constituents of food, 232
- Nodes, Heberden's, 243
- Noise, effect on auditory acuity of aviators, 36
- Nose
 diseases of, 52, 317
 drugs for, 334
 obstruction, treatment of, 317
- Notoedrus cati*, 390
- Novocain, herpes zoster treated by injection of, 256
- Nuck, hydrocele of canal of, 330
- Nupercaine, ocular sensitivity to, 338
- Nutrition, wound healing, and, 13
- O
- Obesity. *See* Adiposity
- Obstetrics
 advances in, 16
 posterior pituitary extract in, 16
- Occupation, factor in longevity, 379
- Ocular
 infections, sulphonamides in, 118
 muscles, balance, in aviators, 31
 sensitivity to percaïne, 338
- Ocular pain, retrobulbar injection of proctocaine for, 244
- Oedema, 318
 aetiology, 318
 cardiac, calcium gluconate in, 254
 embarrassment of venous return causing, 318
 hereditary, 318
 legs, of,
 bilateral, 318
 persistent, 318
 lung, of, associated with menstruation, 318
 nephrotic, treatment of, 313, 314
 nutritional, due to jejunocolic fistula, 318
- Oesophagitis, alcoholic, 134
- Oesophagus
 atresia, congenital, 318
 congenital malformations, 318
 diseases, 318
- Oestradiol
 benzoate, carcinogenic action of, 183
 blood pressure, effect on, 382
 desoxycorticosterone acetate for normal infants, and, 335
 menopausal symptoms treated by implantation of, 190
- Oestrin, menopausal symptoms treated by, 191
- Oestrogen
 effects on cancer tissue, 183
 fibromyomas after injections, prevention of, 383
 gonorrhoeal salpingitis treated with, 228
 lactation, effect on, 383
 new derivatives, 335
 pituitary and pancreas, action on, 382
 rôle in union of fractures, 211
 synergism with pituitary gonadotropins, 384
 uterine bleeding, in, 21
 vaginitis, senile, treated by, 429
- Oestrogenic substances, carcinogenic action of, 183
- Oestrone
 diabetes mellitus during menopause treated by, 191
 menopausal symptoms treated by implantation of, 190
- Oestrous cycle, in cats, effect of light on, 384
- Oidium albicans*, 285

INDEX

- Oil
aspiration (lipid) pneumonia, 177
sulphonated, as detergent in dermatitis venenata, 203
wintergreen, of, fatal poisoning by, 409
Old age. *See also* Longevity; Senescence; Senility
appendicitis in, 148
care of aged poor, 379
diseases in, 380
fibrositis in, 229
gastro-intestinal symptoms in, 380
normal, 379
operative risks in, 380
osteoporosis of spine in, 381
pathological, 380
prophylactic effect of pneumococcus polysaccharide in, 355
rheumatic fever, acute, in, 380
rheumatism in, 229, 381
scurvy in, 425
surgery in, 380
syphilitic infection, incidence of, 380
Olecranon, fracture of, 14
Omentum
great, torsion, 125
sarcoma of, 329
Onychorrhexis, 311
Operations, in aged, 380
Ophthalmia
neonatorum, sulphapyridine in treatment, 196
nodosa, aetiology of, 196
Ophthalmoplegia
chronic progressive, 319
exophthalmic, 319
Opiates, effects on nervous system, 338
Opium, pre-anaesthetic sedative for children, as, 143
Opsonic index, cerebrospinal fever, in, 186
Optic
atrophy, tryparsamide therapy in, 162
chiasma, symptom-complexes associated with, 174
Osteitis deformans,
mono-osteitic type, 172
protruded intervertebral disk associated with, 396
Osteoarthritis
complication of fracture of the ankle, as, 211
treatment, surgical, 153
Osteo-arthropathy, pulmonary, 274
Osteoclastoma, treatment by irradiation, 172
Osteomalacia, cataract associated with, 186
Osteomyelitis
acute,
chemotherapy, 172
spine, of, treatment, 397
staphylococcus, 397
sulphathiazole in treatment, 49
Osteopathia condensans disseminata, 171
Osteopetrosis, 171
Osteophytes, hands, of, 243
Osteopoikilosis, 171
Osteoporosis
hyperparathyroidism, in, 322
post-traumatic, treatment of, 173
spine, of, senile, 381
Osteosclerosis fragilis generalisata, 171
- Otitis media
acute,
chemotherapy in, 57
complications, 216
convulsions complicating, 216
treatment by sulphanilamide, 216
aero-, helium-oxygen therapy in, 182
meningitis complicating, 217
treatment, sulphonamides, 118
Otology, 52
chemotherapy in, 56
Otosclerosis, diagnosis of, 201
Ouabaine, heart failure treated by, 254
Ovarian follicle-stimulating hormone, 382
Ovarian hormones, 382
Ovary
carcinoma,
metastatic ureteral obstruction resulting from, 278
primary signet-ring cell, 319
treatment, 320
dermoid cyst,
malignant, 320
traumatic rupture of, 319
diseases, 319
effect of combined administration of prolactin and the pituitary synergist on, 22
granulosa and theca-celled tumours, 320
tumours, 319
clinical types, 319
granulosa and theca-celled, 320
incidence, symptomatology, and prognosis, 319
malignancy and secretion, 319
signet-ring cell carcinoma, 319
teratomas, 320
Oxygen
effect of helium-oxygen mixture on voice, 335
therapy,
asphyxia in new-born, in, 156
migraine, in, 307
want in aviators, 32
Oxytocic substance, presence in blood of pregnant women, 278
Oxyuriasis, 311
children, in, 311
incidence and treatment, 311
N.I.H. swab examination, 312
pathogeny and symptoms, 312
treatment by phenothiazine, 122
Oxyuris vermicularis, 311, 312
appendix, in, 149
- P
- p*-aminobenzoic acid, control of sulphathiazole therapy by, 344
Paediatrics, 48
Paget's disease of bone, mono-osteitic type, 172
Pain
anginal, 144
cobra venom for relief of, 419
coronary thrombosis, in, 145, 146
hands and feet in acromegaly, 129
intermenstrual, 21
measurement of thresholds for, 320
ocular, retrobulbar injection of proctocaine for, 244

INDEX

- Pain—*continued*
 relief by prostigmin methylsulphate and morphine, 338
 shoulder, associated with myocardial infection, 249
 visceral, associated with dextrocardia, 246
- Palm oil, red, 308
- Pamaquin, 112
- Pancoast tumour of lung, 294
- Pancreas
 action of oestrogens on, 382
 calculi, 321
 carcinoma of head of, 321
 cysts, 321
 diseases, 321
 secretion test in diagnosis of, 322
 inflammatory conditions, 321
 tumours, 321
- Pancreatitis, acute haemorrhagic, diabetes mellitus complicating, 321
- Pantocaine, 113
- Pantothenic acid, riboflavin deficiency and, 424
- Papaverine, benzyl - β - dimethylamino - α - phenyl - α - ethylpropionate hydrochloride compared with, 333
- Papilla, 'snow-capped', 312
- Parachute descents, 33
- Paraffin
 liquid,
 absorption into tissues, 337
 paraffinoma resulting from use of, 330
 pack in treatment of pulmonary tuberculosis, 293
- Paraffinoma, result of liquid paraffin treatment, as, 330
- Paraldehyde, analgesia in labour, 280
- Paralysis
 agitans,
 treatment,
 quinine, 322
 vitamin B₆, 5, 322
 hemi-diaphragmatic, in pulmonary tuberculosis, 292
 herpes zoster causing, 256
 hysterical, in soldier, 363
 Parrot's pseudo-, 404
- Paranoia, clinical picture, 365
- Paraplegia, measles complicated by, 302
- Parasites
 intestinal, treatment by phenothiazine, 122
 skin diseases due to, 390, 391
- Parasympathomimetic drugs, 346
- Parathyroid
 extract, thrombocytopenic purpura treated by, 241
 gland, diseases, 322
 tetany, psychosis complicating, 322
- Paredrine
 intravenous drip administration, 346
 shock, in, 389
- Paredrinol
 effect on circulation, 388
 experimentally produced shock, in, 388
- Parinaud's oculo-glandular syndrome, 109
- Parkinsonism
 encephalitis epidemica causing, 220
 treatment by syntropan, 220
- Parotid gland
 diseases, 323
- Parotid gland—*continued*
 mixed tumours, total parotidectomy for, 323
- Parotidectomy, total, 323
- Parrot's pseudo-paralysis, 404
- Pasteurella tularensis*, 415, 416
- Patent ductus arteriosus, 2
- Paul-Bunnell test, glandular fever, in, 235
- Pavex machine, treatment of compression injuries, in, 9
- Pectoralis major muscle, fixation of, malignant tumours of breast, in, 176
- Pediatrics, 4
- Pediculosis, treatment of, 391
- Pellagra, 324
 aetiology, 324
 alcoholism, chronic, and, 324
 morbid anatomy and pathology, 324
 pellagra-like condition associated with diabetes mellitus, 206
 peripheral nerves in, 324
 'sore mouth' and, 308
 treatment,
 vitamin B, 324
 vitamin C, 324
- Pelvic infection, iontophoresis in, 217
- Pemphigus, 324
 acute, complicating chicken-pox, 189
 neonatorum, carrier of, 325
 solitarius cicatrisans, 325
 vulgaris, treatment by dihydrotachysterol, 324
- Penicillin, 6, 119
 actions of, 119, 120
 antiseptic snuff, as, 331
 chemotherapeutic properties of, 338
 therapeutic trials, 120
- Penicillium notatum*, 6, 119
- Penis
 carcinoma, radium therapy, 325
 diseases, 325
 elephantiasis, surgical treatment, 325
- Peptic ulcer, 326
 aetiology, 326
 age influence, 326
 alkali poisoning in, 135
 aviators, in, 160
 childhood, in, 326
 clinical picture, 326
 complications, treatment of, 328
 histamine factor, 326
 pathology and morbid anatomy, 326
 perforations, simultaneous, 326
 smoking, relation to, 326
 soldiers, in, 214, 215
 stomach and duodenum, 326
 treatment, 326
 aluminium hydroxide, 327
 aluminium phosphate gel, 327
 bleeding ulcers, of, 328
 colloidal aluminium hydroxide, 327
 complications, of, 328
 gastric resection and acidity, 327
 magnesium trisilicate, 328
 Meulengracht régime, 328
 partial gastrectomy, 326
 syntrogeol, 327
 vitamin A (avoleum), 327
- Perandren, blood pressure, effect on, 382
- Percaïne, ocular sensitivity to, 338

INDEX

- Periarteritis nodosa, 151
 Pericarditis
 rheumatic, salicylate therapy, 248
 sulphathiazole in treatment, 49
 Pericardium
 diseases, 248
 Perineal anaesthesia, in labour, 280
 Perisymphathetic injection, in treatment of
 asthma, 158
 Peritoneal cavity
 introduction of sulphanilamide into, 272
 paraffinomas as result of liquid paraffin
 treatment, 330
 Peritoneum
 non-inflammatory diseases, 329
 tumours, 329
 Peritonitis
 acute, treatment by alcohol lavage, 330
 adhesive, 330
 chronic, 330
 encapsulating, 271
 local application of sulphonamides in, 13
 Permanent waving, hydrogen sulphide
 poisoning during, 410
 Pernicious anaemia
 aetiology, 139
 erythrocyte response to treatment, 139
 plasma-prothrombin in, 139
 treatment, 139
 vitamin K plasma-prothrombin relation,
 139
 Personality, types, and effort syndrome, 245
 Petechial haemorrhages, anti-syphilitic
 therapy causing, 405
 Pethidine hydrochloride, 113
 Petroleum jelly dressings, 264
 Phagedaenic ulcer, 392
 Pharmacology, 330
 Pharmacopoeia, British
 additional monographs, 112
 Fourth Addendum to, 112
 Pharmacy and Medicines Act (1941), 111
 Pharyngitis, acute, and Vincent's angina,
 349
 Pharyngo-oesophageal sphincter, achalasia
 of, 128
 Pharynx
 carcinoma of tonsil, 349
 diseases, 349
 infections of, chemotherapy in, 60
 polypoid fibro-lipomatosis pharyngis, 349
 tumours, 349
 ulcers, decubital, 350
 Phenobarbitone
 belladonna, and, epilepsy treated by, 222
 exfoliative dermatitis due to, 204
 Phenolphthalein
 effect on liver, 288
 test, in detection of ulceration of gastro-
 intestinal tract, 273
 Phenothiazine
 anthelmintic, as, 122
 treatment of ascariasis, in, 156
 Phenovis, 122
 Phenytoin, soluble, 113
 Phlegmasia alba dolens, 296
 Phosphatase, production, in tumours of
 bone, 172
 Phosphorus, metabolism, in toxic goitre, 236
 Phrenazol, 79. *See also* Cardiazol
 Phrenic nerve, paralysis, pulmonary tuber-
 culosis, in, 292
 Phrenico-costal sinus pneumonia, 298
 Physiotherapy, 350
 general practice, 350
 refrigeration, 350
 rheumatoid arthritis, 154, 155
 Pili torti, 243
 Pilots. *See* Aviation medicine; Aviators;
 Flying
 Pineal body, tumours, 350
 Pinelectomy, experimental, results of, 350
 Pingueculae, biopsy examination of, in
 Gaucher's disease, 287
 Pink disease, vitamin B₁ in treatment, 50
 Pitressin
 effects in cardiovascular disease, 336
 tannate, diabetes insipidus treated by,
 205
 Pituitary
 extract,
 anterior lobe, 22
 anti-diabetogenic principle, 205
 gonadotrophic, antagonism to pregnant
 mare serum, 336
 induction of labour, in, 279
 posterior lobe,
 diabetes insipidus treated by, 205
 induction of labour, in, 279
 gland,
 action of oestrogens on, 382
 diseases, 351
 hormones,
 anterior lobe, 351, 382
 growth hormone, 351
 ovarian follicle-stimulating, 382
 purified interstitial cell-stimulating,
 351
 synergism of oestrogens with pituitary
 gonadotropins, 384
 thyroidotrophic, 382
 Laurence-Moon-Biedl syndrome, 351
 physiology, 351
 posterior lobe,
 fractured skull and injury to, 174
 gastric changes following injury to,
 174
 preparations, posterior, in obstetrics, 16
 synergist, 22
 Pituitrin, in blood of pregnant women,
 278
 Placenta
 luteinizing principle from, 22
 visualization by soft-tissue radiography,
 280
 Placental extract, prophylaxis of measles, in,
 302
 Plantar warts, X-rays and radium therapy
 for, 393
 Plants, dermatitis caused by, 202
 Plasma-fibrinogen, in repair of peripheral
 nerve lesions, 94
 Plasma-prothrombin
 pernicious anaemia, in, 139
 titrations in infants, 241
 Plasmoquine, 112
 Plaster of Paris
 bacteriology of wounds treated by closed
 method, 267
 'windowed' unpadded casts, 265

INDEX

- Plastic surgery, 12
sutures, synthetic, 264
- Plethysmographic method of measuring peripheral blood-flow, 151
- Pleura, diseases, 71
- Pleural effusion,
radiography in, 352
tuberculous, eosinophilia in, 291
- Pleurisy, 352
- Plummer-Vinson syndrome, radiological observations, 128
- Pneumococcal meningitis. *See* Meningitis, pneumococcal
- Pneumococcus
infection,
sulphapyridine in, 342
sulphonamides in, 342
metabolism, effect of sulphonamides on, 342
polysaccharide, in prophylaxis of pneumonia, 355
- Pneumonia, 3
aspiration, 177
clinical picture and treatment, 177
lobar, 352
children, in, 355
course and prognosis, 352
infants, in, 352
mortality and sulphonamide compounds, 352
pneumococcal, 352, 353
prophylactic effect of pneumococcus polysaccharide in old age, 355
sputum, 352
treatment, 352
combined chemotherapy and serum therapy, 354, 355
cortin and sodium chloride, 355
hydroxyethylapocupreine and sulphapyridine, 354
sodium sulphapyridine intravenously, 354
sulphapyridine, 353, 354
sulphathiazole, 352, 353, 354
sulphonamides, 352
X-ray, 355
phrenico-costal sinus, 298
treatment,
sulphathiazole, 177
sulphonamide compounds, 177
young adults, 177
- Pneumothorax
artificial, results and complications, 293
embolism causing, 290
pulmonary infarction causing, 290
- Poisoning, 408
homicidal, suicidal, and accidental, 408
industrial, 411
- Poison-ivy dermatitis, 203
- Poisons, 408
- Polio-encephalitis, Wernicke's, vitamin B deficiency associated with, 369
- Poliomyelitis, 356
aetiology, 356
antibodies, formation of, 356
epidemiology, 356
field of contagion in children, 356
immunity and resistance, 356
- Poliomyelitis—*continued*
olfactory mucosa in, 356
stools, toxic factor in, 356
tonsillectomy and, 356
treatment,
potassium chlorate, 357
serum injections, 357
sulphapyridine and anti-serum, 356
sulphonamides, 49
- Pollen
contact, and age of onset in hay fever, 137
extract,
skin sensitivity, and, 137
slow-absorbing, in hay fever, 136
oral, in treatment of hay fever, 137
- Polycystic disease of kidney, 275
- Polycythaemia, experimental, 225
- Polyneuritis. *See* Neuritis, multiple
- Polypi
colon, multiple primary, 195
intestinal, 375
- Polypoid fibro-lipomatosis pharyngis, 349
- Polyposis
intestine, of, 375
differential diagnosis, 375
precursor of carcinoma, 375
- Polyradiculitis, mumps complicated by, 309
- Polysaccharides, antigenic capsular, in prophylaxis of pneumonia, 355
- Poor, aged, care of, 379
- Porphyrins, excretion, in methyl chloride poisoning, 411
- Portal vein, pylephlebitis, suppurative, 288
- Postural hypotension, 166, 167
- Posture, treatment of shock, in, 387
- Potassium
chlorate, poliomyelitis treated by, 357
chloride,
treatment of allergic diseases, 136
treatment of extrasystoles, 150
salts and anuria, 408
tolerance curve, diagnosis of Addison's disease, in, 131
- Pott's disease, 396
- Precancerosis, 394
leucoplakia and keratoses, 394
- Precocity, interstitial celled tumour of testis and, 405
- Pre-eclampsia, hypertension and, 18
- Pre-frontal lobotomy, treatment of mental disease by, 365
- Pregnancy
adrenal haemorrhage in, 358
blood in, oxytocic substance and pituitrin, 278
diabetes mellitus in, 16
diagnosis, 357
antuitrin-S skin test, 357
Friedman test, 358
urinary excretion of pregnanediol, 357
xenopus test, 358
diphtheritic antitoxin level in, 260
ectopic, and pre-existing tubal infection, 228
haemorrhages of, 358
hormones in, 357
hyperemesis gravidarum, 358
hypoparathyroidism in, 323
oxytocic substance and pituitrin in blood, 278

INDEX

- Pregnancy—continued**
 physiology, 357
 posterior pituitary preparations in, 16
 pregnanediol excretion, 357
 pregnanediol excretion during, 18
 pyelitis of, 19
 soft-tissue radiography in, 280
 stilboestrol, effects of, 383
 toxæmias of, 358. *See also* Eclampsia
 classification of, 18
 nephrosclerosis and, 357
 pre-eclampsia and eclampsia and renin, 18
 tubal. *See* Tubal pregnancy
 vomiting of, 358
 X-ray examination in, 280
- Pregnanediol**
 excretion after removal of ovarian tissue, 357
 excretion during pregnancy, 18
 urinary excretion in pregnancy, 357
- Pregneninolone**, treatment of abortion, in, 126
- Pre-senile and senile psychoses**, 84
- Pressor substances**, 165, 166
 eclampsia, and, 18
- Printers**
 benzene poisoning in, 411
 lead poisoning in, 282
- Procaine**
 adrenaline, and, 112
 injections for sprains, 159
 hydrochloride,
 injection into scalenus anticus muscle, 189
 local anaesthetic, as, 142
- Proctocaine**, ocular pain treated by retro-bulbar injection of, 244
- Profession**, as factor in longevity, 379
- Proflavine**
 antiseptic snuff, as, 331
 bacteriostatic value, 330
 prevention of nasal sepsis and post-operative scarlet fever, 330
- Progesterone**
 diabetes mellitus during menopause treated by, 191
 implantation of, 384
 menstrual and climacteric disorders treated by, 384
- Progyonon**, blood pressure, effects on, 382
- Prolan**
 effect on human ovary, 22
 effect of large dosage of, 22
 pituitary synergist and, 22
- Promin**, 119
 blood levels, 337
 effect on experimental tuberculosis, 336
 streptococcal infection, in, 336
- Prontosil**, therapy, trachoma, 412
- Propadrine hydrochloride**, intravenous drip administration, 346
- Proprietary drugs**, names of, 113
- Prostate**
 calculi, trans-urethral removal, 361
 carcinoma, direct extension to ureter in, 361
 diseases, 359
 enlargement, simple, 360
 diagnosis, 360
 differential diagnosis, 360
 incidence, 360
- Prostate—continued**
 enlargement—*continued*
 largest recorded prostate, 360
 pyelography, intravenous, in, 360
 treatment, testosterone propionate, 360
 X-ray examination, 360
 malignant disease, 361
 tuberculosis, 359
- Prostatitis**, treatment with staphylococcus toxoid, 359
- Prostigmin**
 chronic deafness treated by, 201
 methylsulphate,
 deafness and tinnitus aurium treated by, 201
 morphine in relief of pain, with, 338
- Protein**
 serum, 305
 cases of wounds, in, 263
 relation to wound healing, in, 268
- Prothrombin**
 deficiency, post-operative, in obstructive jaundice, 273
 estimation by Russell's viper venom technique, 163
 level, effect of vitamin K, 427
 plasma, in pernicious anaemia, 139
 time in new-born, effect of vitamin A, 427
- Protozoal disease**, diamidines in, 100
- Prurigo**
 annularis, 361
 hebra, 361
- Pruritus**
 ani, faecal soiling of perianal skin and, 147
 vulvae, use of stilboestrol cream, 430
- Pseudo-appendicitis**, rheumatic, 378
- Pseudo-fractures of bone**, 171
- Pseudo-laryngocele**, 311
- Pseudomonas pyocyanea***, wounds infected by, 267, 268
- Pseudo-paralysis**, Parrot's, 404
- Psittacosis**, treatment by sulphapyridine, 361
- Psoriasis**, 362
 aetiology, 362
 metabolic disturbances in, 362
 nails, X-ray therapy for, 362
 syphilitic skin lesions resembling, 403
 treatment,
 vitamin P, 362
 X-rays, 362
- Psychiatry**, 79
 children, of, combined subjective and objective disorders, 362
 research in, 83
 war, 85, 86
- Psychological**
 factors, deafness, in, 201
 reactions in acne vulgaris, 128
 tests, for aviators, 32
- Psychoneuroses**, 362
 aetiology, 362
 air-raids, civilian reactions to, 363
 compulsion, leptazol therapy, 364
 evipan analysis in, 259
 hypnosis in investigation of, 259
 obsessive-compulsion, leptazol therapy, 364
 traumatic experiences, reactions to, 363
 war, influence of, 85, 86, 363
- Psychopathology**, psychotherapy and, 83

INDEX

- Psychoses**
 affective, 364
 aetiology, 364
 sex hormones, rôle of, 364
 treatment, 365
 endocrines, 365
 non-convulsant, 365
 pre-frontal lobotomy, 365
 sub-convulsant therapy, 365
 alcoholic, 369
 cerebrospinal fluid pressure in, 188
 cerebrospinal fluid pressure in, 188
 parathyroid tetany complicated by, 322
 traumatic, 363
Psychotherapy, 362
 menopausal symptoms, in, 191
 psychopathology and, 83
Puerperal sepsis, treatment by sulphonamides, 370
Puerperium, 370
 ergometrine treatment, 370
 normal, management of, 370
 physiology, 370
 sterilization in, 22
 thrombosis of cerebral veins in, 407
 uterus, effect of stilboestrol on, 370
Pulmonary
 artery, aneurysm of, 144
 eosinophilia, 157
 osteo-arthritis, 274
 stenosis, aortic aneurysm and, 143
 tuberculosis. *See* Tuberculosis, pulmonary
Pulse, response test, 244
Purpura
 haemorrhagica, arsphenamines causing, 213
 meningococcal septicaemia associated with, 186
 rheumatism associated with, 241
 simplex, familial, rheumatism associated with, 241
 thrombocytopenic,
 aetiology, diagnosis, and treatment, 241
 measles complicated by, 302
 sulphapyridine causing, 343, 344
 treatment with parathyroid, 241
 vitamin P therapy in, 241
Pyelitis, of pregnancy, 19
Pyelography
 excretion, uroselectan B in, 371
 intravenous, in prostatic disease, 360
Pyelonephritis
 hypertension and, 165
 unilateral atrophic, and malignant hypertension, 165
Pylephlebitis, thorium dioxide in diagnosis, 288
Pyloric
 obstruction, 370
 stenosis,
 acidosis associated with, 128
 blood changes in, 128
 congenital, operative treatment of, 13
 eumydrin in treatment of, 4, 50
 hypertrophic, treatment by eumydrin, 370
Pyrethrum, dermatitis caused by, 202
Pyretotherapy
 chorea, in, 189
 disseminated sclerosis, 212
Pyretotherapy—continued
 general paralysis of insane, in, 315
 general paresis, in, 105
 gonorrhoea, in, 238
 sulphonamides with, 108
Pyridoxin, 5, 423. *See also* Vitamin B₆
 hydrochloride. *See* Vitamin B₆
Pyuria
 children, in, 418
 chronic, congenital anomalies of urinary tract and, 231

Q

- Quartz-rod transillumination**, intrahepatic circulation observed by, 288
Quinine
 paralysis agitans treated by, 322
 urethane, and, 112
Quinine-insulin mixture, diabetes mellitus treated with, 207
Quinocaine, in staphylococcal infection, 339

R

- Radio-dermatitis**, surgical treatment of, 202
Radiographic examination. *See* X-ray examination
Radiography, mass, 75, 76. *See also* X-ray examination
Radiology, 371. *See also* Radiotherapy;
 Radium therapy; X-ray examination;
 X-ray therapy
Radionecrotic ulcers, zinc treatment, 372
Radiotherapy, 372
 cancer, 184
 quantitative examination of biopsy material in, 184
 treatment of surrounding tissue, 185
 carcinoma of breast, 176
 clinical applications, 373
 malignant disease, 184
 radionecrotic ulcers, zinc treatment, 372
 skin diseases, 373
 uterine fibromyomas, 419
Radium therapy, 373
 birth-marks, 373
 carcinoma,
 breast, of, 176
 cervix uteri, of, 419
 penis, of, 325
 clinical applications, 373
 plantar warts, 393
Rammstedt, operation, 13
Rash, sulphonamides causing, 344
Raspberry leaves, relief of labour pains by, 20
Rat-bite fever, fatal termination, 374
Raynaud's phenomenon
 clinical picture, 374
 sclerodactyly (acrosclerosis), in, 374
 scleroderma and pulmonary fibrosis in, 375
Recruits
 cardiovascular diseases in, 44
 examination of, 44
 heart, 2
 heart disease in, 244, 245
Rectal administration
 drugs, of, absorption and excretion, 339
 sulphanilamide, of, 343
Rectal surgery, 14

INDEX

- Recto-vaginal septum, endometriosis of, 221
- Rectum
- carcinoma, X-ray treatment without colostomy, 375
 - diseases, 375
 - drugs administered by, 339
 - polyposis,
 - differential diagnosis, 375
 - precursor of carcinoma, 375
 - simple ulcers of, 193
 - sulphanilamide administered by, 343
 - surgery of, 14
 - tumours,
 - benign, 375
 - malignant, 375
- Red hair, and susceptibility to tuberculosis, 414
- Reflexes
- Babinski's, 376
 - crossed plantar responses, 376
 - diagnosis, in, 376
 - fundus oculi, of, 227
- Refrigeration
- cancer treated by, 184, 350
 - general and local, 350
 - local, in treatment of carcinoma of cervix uteri, 419
 - morphine addiction treated by, 350
- Rehabilitation, 8
- after coronary occlusion, 146
- Renal
- colic, sulphonamides causing, 116, 346
 - complications, due to sulphathiazole, 343
 - extract, in treatment of renal hypertension, 166
 - function, impairment in crush injuries, 269
 - hypertension, 165
 - insufficiency,
 - blood transfusion causing, 170
 - prolonged, complicating hyperparathyroidism, 323
 - ischaemia and hypertension, 2, 3
- Rendu-Osler syndrome, 223
- Renin
- eclampsia, and, 18
 - effect of nephrectomy on pressor response to, 166
 - rôle in hypertension, 165
- Reparative or restorative surgery, 12
- Respiration
- artificial, 212
 - heart disease, in, effect of coramine on, 334
- Respiratory
- diseases, 3
 - tract,
 - Hodgkin's disease, 258
 - upper, infections of, in relation to asthma, 157
 - upper, streptococcal infections and rheumatic fever, 377
- Resuscitation, in drowning, 212
- Retina
- angiomatosis, treated by catholysis and surface diathermy, 377
 - degenerations of, 162
 - detachment,
 - aetiology, 377
 - surgical treatment, 377
 - diseases, 376
 - tumours, 377
- Retina—*continued*
- varices, in diabetic retinitis, 376
 - vascular diseases, 376
 - venous thrombosis, treated by heparin, 376
- Retinitis
- diabetic, varices in, 376
 - pigmentosa, 376
 - clinical picture, 376
 - treatment by atropine sulphate, 376
- Rhagades, of congenital syphilis, 403
- Rheumatic
- fever. *See also* Rheumatic infection, acute
 - acute, in old age, 380
 - appendicitis, acute, associated with, 377
 - streptococcal upper respiratory infections and, 377
 - sulphonamides in treatment, 49
 - infection, acute, 377
 - association with acute appendicitis in children, 377
 - bacteriology and morbid anatomy, 377
 - cardiac lesions, 377
 - clinical picture, 377
 - diagnosis, two-step test, 378
 - haemolytic streptococci, recovery of, 377
 - juvenile type, 377
 - prophylactic treatment by sulphanilamide, 378
 - recurrences in streptococcal upper respiratory infections, 377
 - treatment, 378
 - pericarditis, salicylate therapy, 248
- Rheumatism
- formol-gel reaction in diagnosis, 154
 - muscular, 229
 - old age, in, 229, 381
 - purpura associated with, 241
 - treatment,
 - heat and Scott's dressing, 229
 - physical methods, 229
- Rheumatoid arthritis
- aetiology, 153
 - cardiac lesions in, 154
 - diagnosis, 154
 - extra-articular lesions, 154
 - focal infection and, 154
 - formol-gel reaction in diagnosis, 154
 - heart disease associated with, 154
 - treatment,
 - bee venom, 155
 - gold salts, 154
 - splints and physiotherapy, 154, 155
 - vitamin A deficiency in, 153
 - X-rays, high voltage, 373
- Rhinitis
- chronic obstructive,
 - sodium morrhuate injections, 317
 - submucosal injections of sodium psylliate, 317
- Rhinorrhoea, cerebrospinal, bifrontal craniotomy for, 188
- Rib, cervical, 189
- Riboflavin
- administration in diabetes mellitus, 206
 - deficiency and pantothenic acid, 424
- Rickets, adult, cataract associated with, 186
- Ringworm, feet and hands, of, preventive treatment, 233
- Rorschach test, 85

INDEX

Rotating
 hexagon for testing night vision, 31
 stereogram, 31
 Rotenone, scabies treated by, 391
Rubus idoeus, extract of, 20
 Russell's viper venom, use in estimation of
 thrombokinas, 163

S

'Safe period', 197
 Salicylates, rheumatic pericarditis treated by,
 248
 Saligenin, neurosyphilis treated by, 316
 Saline
 hypertonic, shock treated by, 388
 transfusions in shock, 387
 Salpingitis, gonorrhoeal, oestrogenic therapy,
 228
 Sand-blasted, acute silicosis in, 389
 Santonin poisoning, 408
 Sarcoidosis, bronchial, 295
 Sarcoids, Boeck's, 394, 395. *See* Boeck's
 sarcoid
 Sarcoma
 arising from a haematoma, 183
 jejunum, of, 272
 Jensen's rat, X-ray therapy, 372
 omentum, of, 329
 uveal tract, of, 420
 Scabies, 391
 pediculosis and, 391
 treatment, 120
 benzyl benzoate, 391
 derris root, 391
 rotenone, 391
 Scalds, 178. *See also* Burns
 Scalenus anticus muscle, procaine hydro-
 chloride injection into, 189
 Scalenus syndrome, 189
 Scalp, wounds, treatment of, 196
 Scaphoid, carpal, internal fixation of frac-
 tured, 211
 Scarlet fever
 diagnosis, 67
 gangrene of feet complicating, 378
 immunization by toxin in tablet form, 378
 nephritis complicating, 313
 post-operative, acriflavine and proflavine
 in prevention of, 330
 prophylaxis, 67
 treatment, 67
 Schick test, bullous reactions in, 209
 Schizophrenia, 366
 classification, 366
 convulsion therapy, 80
 definition and nomenclature, 366
 treatment, 366
 ammonium chloride convulsant therapy,
 368
 electrical convulsant therapy, 368
 faradic shock, 368
 insulin shock, 367, 368
 insulin shock,
 compression fractures of spine, 367
 economical war-time method, 367
 intravenous administration, 368
 leptazol shock therapy, 366, 368
 cardiovascular patients, in, 367
 fractures due to, 366

Schizophrenia—*continued*
 treatment—*continued*
 leptazol shock therapy—*continued*
 memory defects following, 367
 results of, 367
 triazol convulsant therapy, 368
 Schüller-Christian syndrome, 287
 involving middle ear and temporal bone,
 287
 Schumin's test, 170
 Sciatica, dislocation of intervertebral disks
 and, 14
 Sclerodactyly, Raynaud's phenomenon asso-
 ciated with, 374
 Scleroderma
 progressive, relation to dermato-myositis,
 379
 pulmonary fibrosis in Raynaud's pheno-
 menon, 375
 Sclerosis, amyotrophic lateral, 307
 Scoliosis, treatment by conservative methods,
 396
 Scorpion stings, 161
 Scott's dressing, rheumatism treated by, 229
 Scrotum
 diseases, 325
 elephantiasis, surgical treatment, 325
 haemangioma, 325
 mule-spinner's cancer, 392
 tumours, 325
 Scurvy, 5
 aged, in, 425
 infantile, 379
 Secretin test, diagnosis of pancreatic diseases,
 in, 322
 Sedation, tetanus, in, 407
 Sedatives
 barbiturates as, 332
 menopausal symptoms treated by, 191
 pre-anaesthetic, 143
 Sedimentation rate, malignant disease, in,
 163
 Selenium, poisoning, in endemic areas, 410
 Seminoma
 abdominal testis, of, 405
 teratoma and, concurrent, 405
 traumatic displacement of testis resulting
 in, 405
 Senescence, 379. *See also* Old age
 Senile
 keratoderma, 191
 osteoporosis of spine, 381
 toxic exhaustion syndromes, treatment of,
 82
 Senility, 379
 Sepsis, puerperal. *See* Puerperal sepsis
 Septicaemia
 chemotherapy in, 58
 gonococcal, 237, 238
 meningococcal, 4
 staphylococcal, sulphathiazole in, 342
 streptococcal, sulphathiazole in, 342
 treatment, sulphonamides, 115
 Septum
 interauricular, defects of, 247, 248
 interventricular, rupture of, due to cardiac
 infarction, 146
 recto-vaginal, endometriosis of, 221
 ventricular, transposition of great vessels
 with defect of, 248

INDEX

- Serum
 protein, 305
 concentration in cases of wounds, 263
 wound healing, relation to, 268
 therapy,
 anthrax, 147
 cerebrospinal fever, 187
 chemotherapy in pneumonia, and, 354,
 355
 convalescent serum,
 measles, in, 302
 poliomyelitis, 356
 pneumonia, 354, 355
 poliomyelitis, 356, 357
 Sex factor in longevity, 379
 Sexual behaviour and abnormalities, 385
 Sheep, ecthyma contagiosum, virus disease
 of, 217
 Shock, 1, 8, 385
 adrenal secretions, rôle of, 386
 anaesthetics, choice of, 388
 blood pressure in, 1, 40, 41
 blood transfusion in treatment of, 38
 burns, in, 179, 180
 cortin, pre-operative administration of,
 387
 estimation of degree of, 1
 experimental, paredrinol in, 388
 fat embolism and, 386
 histamine-like substance, rôle of, 386
 hypotheses of, 386
 indications for operation in, 9
 injury and, 386
 neurogenic hypothesis, 386
 primary, 38
 restoration of blood volume in, 1
 review of published records on, 39
 secondary, 38, 387
 surgical,
 heat and cold, effect of, 387
 treatment of, 387
 therapy. *See* Convulsion therapy; Insulin
 shock therapy
 traumatic,
 nervous factor in, 386
 splenectomy, effect of, 386
 thrombocytopenia in, 386
 treatment, 9, 387
 hypertonic saline, 388
 intravenous transfusions, 387
 paredrinol, 388
 plasma and blood transfusion, 387
 pooled concentrated human serum, 388
 postural, 387
 pre-operative administration of cortin,
 387
 saline and serum, intravenous trans-
 fusions, 387
 transfusion and a vasoconstrictor, 388
 wound, 39
 Short-wave therapy, dental sepsis, in, 202
 Shoulder pain
 associated with myocardial infection, 249
 use of procaine hydrochloride in, 189
 Siccolam, use in skin lesions, 339
 Sickness, air, 36
 Sideropenic dysphagia, 128
 Silicosis, 389
 acute, 389
 aetiology, 389
 Silicosis—*continued*
 clinical picture, 389
 miners of bituminous coal, in, 389
 morbid anatomy, 389
 sand-blasted, rapid onset in, 389
 tuberculo-, X-ray findings, 390
 Silk sutures in infected wounds, 266
 Silver
 ferrihaemoglobin, ophthalmic and oto-
 rhino-laryngological conditions,
 339
 nitrate, burns treated with, 181
 Simmonds's syndrome, spontaneous hypo-
 glycaemia in, 92, 390
 Sinus
 carotid, 2
 frontal, infection, spreading, 127
 lateral venous, congenital absence of, 216
 maxillary, lipiodol radiography, 127
 nasal accessory, 127
 lipiodol radiography, 127
 thrombophlebitis, heparin and sulphona-
 mide therapy, 408
 Sinusitis
 acute,
 frontal, infection after, 127.
 X-ray therapy, 127
 bronchiectasis, relation to, 127
 chronic,
 sodium salt of sulphathiazole in, 127
 X-ray therapy, 127
 treatment,
 sodium salt of sulphathiazole, 127
 X-rays, 127
 Skeleton
 leukaemia, in, 286
 X-ray examination, 371
 Skin
 abnormalities, 230
 action of various drugs on, 331
 allergy of, 137
 amoebiasis of, 138
 Boeck's sarcoid, 394, 395
 cancer, mule-spinner's, 392
 carcinoma,
 significance of skin colour, 394
 X-ray treatment, 394
 colour, and cancer, 394
 dermatofibroma, 393
 diseases, 390
 locally inoculated infections, 392
 occupational, 392
 siccolam, use of, 339
 sulphapyridine in, 342
 treatment, 120
 treatment by siccolam, 339
 X-ray therapy, 373
 eruptions, sulphonamides causing, 344
 gangrene, progressive, 392
 glomus tumours, 393
 grafting, 264
 innocent infective conditions, 394
 keratoses, 394
 leucoplakia, 394
 necrobiosis lipoidica diabetorum, 395
 necrosis, spreading, 392
 precanceroses, 394
 pre-operative preparation of, 331
 sarcoids, multiple benign sarcoid of
 Boeck, 394, 395

INDEX

Skin—continued

- skin-*See also War*
 sulphapyridine eruptions, 213
 systemic conditions, 395
 tumours, 393
 derived from fibrous tissue, 393
 derived from hair follicles, 393
 derived from nerve tissue, 393
 derived from superficial layers, 393
 innocent, 393
 malignant, 394
 precanceroses, 394
 Skull fracture, and injury to posterior
 pituitary, 174
 Sleep
 disorders, 85
 recorders, 85
 Smoking
 coronary disease and, 152
 gastric acidity, effect on, 326
 thrombo-angiitis obliterans and, 151
 Snake venom, herpes simplex treated by, 256
 Snuffs, antiseptic, 331
 Sodium acid sulphate, poisoning by, 408
 Sodium amylal, use in convulsion therapy, 79
 Sodium ascorbate, intravenous injections of,
 in haemorrhage, 269
 Sodium bicarbonate
 treatment of scorpion stings, in, 161
 vitamin C in treatment of erythraemia,
 and, 225
 Sodium chloride
 bromide eruptions treated by, 213
 pneumonia treated by cortin and, 355
 Sodium compounds of sulphonamides, 340,
 346
 Sodium diphenylhydantoinate, 113
 compared with other anti-convulsive drugs,
 222
 effect of large doses, 339
 epilepsy treated with, 222
 infantile convulsions treated by, 197
 toxic effects in mentally defective, 223
 Sodium hypochlorite, treatment of burns, in,
 114
 Sodium morrhuate, 112
 injections in chronic obstructive rhinitis,
 317
 sensitivity to, 421
 Sodium psylliate, submucosal injections of,
 in chronic obstructive rhinitis, 317
 Sodium salicylate, absorption and excretion
 after rectal administration, 339
 Sodium succinanilomethylamide-*p*-arsonate.
 See Neocryl
 Sodium sulphamethylthiazole, urinary tract
 complications due to, 346
 Sodium sulphapyridine
 cerebral symptoms arising from, 187
 intravenously, in lobar pneumonia, 354
 treatment of cerebrospinal fever, 187
 urinary tract complications due to, 346
 Sodium sulphate, hypertonic, and acriflavine,
 in infected wounds, 268
 Sodium sulphathiazole, urinary tract com-
 plications due to, 346
 Sodium thiosulphate, effect on excretion of
 arsenic, 404
 Sodium thorium tartrate, use in radiography,
 371
 Soft-tissue radiography, pregnancy, in, 280

INDEX

- Splint
rheumatoid arthritis, in, 154, 155
vitalium, use of, 210
- Spondylarthritis ankylopoietica, 155
- Spondylitis, ankylosing, 155
- Spondylolisthesis, fourth lumbar vertebra, of, 161
- Spore-forming bacteria in milk, 232
- Spotted bones, 171
- Sprains, procaine injections for, 159
- Spray, intranasal vaccine, in prevention of colds, 193
- Sprue, 26, 398
aetiology, 398
fat absorption, mechanics of, 26
lacteal obstruction and, 28
morbid anatomy, 27
non-tropical, 26. *See* Coeliac disease
paralysis of muscularis mucosae, 27
pathogenesis of, 26
stools in, 26
treatment, nicotinic acid, 399
valvulae conniventes in, 27
- Sputum
lobar pneumonia, in, 352
pulmonary tuberculosis, in, 292
- Staining, supravital, of leucocytes, 7
- Staphylococcus
infection,
glucose tolerance and, 306
neoarsphenamine in, 342
quinocaine in, 339
sulphonamides in, 342
toxoid, prostatitis treated with, 359
- Staphylococcus aureus*,
infections, sulphonamides in, 342
wounds infected by, 267, 268
pyogenes, in pemphigus neonatorum, 325
- Status asthmaticus, fatality during, 158
- Steatorrhoea
hypovitaminosis of fat-soluble vitamins in, 192
idiopathic, 26
haemorrhagic diathesis associated with, 192
vitamin K deficiency in, 192
- Stenosis, pyloric. *See* Pyloric stenosis
- Stereoscopic vision in relation to landing of aircraft, 31
- Sterility, 21, 399
female,
effect of pus on survival of spermatozoa, 399
treatment by tubal insufflation, 399
male,
testicular biopsy, 399
treatment by pregnant mare serum, 400
- Sterilization
puerperium, in, 22
solutions intended for injections, of, 113
- Sternal puncture, 6, 7
Gaucher's disease, in, 287
- Sternum, suprasternal bones, 371
- Stibophen. *See* Fouadin
- Stilboestrol
carcinogenic action of, 183
cream, in treatment of pruritus vulvae, 430
early pregnancy, in, 383
- Stilboestrol—*continued*
effect on post-partum uterus, 370
gynaecomastia in male caused by, 383
hepatotoxic effect, alleged, 383
inhibition of lactation by, 262
menopausal symptoms treated by, 191
- Stings, scorpions, 161
- Stokes-Adams syndrome
electrocardiogram in, 246
heart-block and, 246
- Stomach
carcinoma,
depressant effect of carcinoma extracts on gastric secretion, 401
dual (kiss) carcinoma, 400
presence of spirochaetes in gastric mucosa, 401
termination by Lederer's acute haemolytic anaemia, 401
treatment,
total gastrectomy and partial oesophagectomy for, 401
total gastrectomy technique, 401
changes, following injury to posterior pituitary, 174
diverticula of cardiac end, 402
surgery of, 14
syphilis of, 234
tuberculous ulcers, 401
tumours, malignant, types of, 400
ulcer. *See* Gastric ulcer; Peptic ulcer
- Stomatitis, treatment by chromium trioxide, 307
- Stools. *See* Faeces
sprue, in, 26
- Strabismus, 402
children, in, 402
comitant, 402
lacquered lenses, use of, 402
non-paralytic, 402
- Streptococcal infections, Dick test, reliability of, 261
- Streptococcus
haemolytic,
Dick test in infections, 261
recovery in cardiac lesions of acute rheumatism, 377
infection, promin in, 336
respiratory infections and rheumatic fever in children, 377
viridans infection,
bacterial endocarditis, treatment, 251
recovery, with, 250
- Streptococcus pyocyanea*, wounds infected by, 267
pyogens, wounds infected by, 268
viridans, meningitis caused by, 304
wounds infected by, 267
- Stromal tumours of choroid plexus, 175
- Strophantin, electrocardiogram changes due to, 340
- Subacromial bursitis, 189
- Subacute combined degeneration. *See* Spinal cord
- Subarachnoid, injections of alcohol, for relief of intractable pain, 185
- Subclavian veins, thrombosis of, 420, 421
- Subdeltoid bursitis, 189
- Suction treatment of boils and carbuncles, 171

INDEX

'Sulcus tumour' of lung, 294
 Sulphaceamide, 113
 Sulphadiazine, 6, 119
 absorption, excretion, and distribution, 340, 341
 therapy, 341
 Sulphaguanidine, 6
 treatment, typhoid fever, 222
 Sulphamethylthiazole, 117
 encephalopathy following administration of, 175
 local application in wounds, 267
 therapy, staphylococcal infection, 342
 toxic reactions, 343
 treatment,
 gonorrhoea, 238
 puerperal sepsis, 370
 Sulphanilamide
 anaemia, secondary, produced by, 344
 haemoglobinuria caused by, 240
 intrapertitoneal, in treatment of intestinal obstruction, 272
 liver necrosis and, 343
 local application in wounds, 266, 267
 myopia caused by, 310
 preservative for blood, as, 169
 rectal administration, 343
 therapy,
 clostridium welchii infection, 341
 gas gangrene, 341
 rheumatic infection, acute, 378
 staphylococcal infection, 342
 trachoma, 412
 urinary infections, 344, 345
 toxic effects, 240
 treatment of, in,
 acute osteomyelitis, 172
 bites, human, 269
 chancroid, 189
 erysipelas, 224
 fractures, 210
 inclusion conjunctivitis, 196
 intestinal obstruction, 272
 laryngo-tracheobronchitis, 281
 otitis media, 216
 ulcerative colitis, 194
 Sulphanilylguanidine, 119
 dysentery treated by, 65
 treatment of bacillary dysentery, 213
 Sulphapyridine
 agranulocytosis caused by, 134, 343, 344
 anuria caused by sulphapyridine calculi, 161
 calculi, 161
 children's diseases treated by, 48
 heparin and, in bacterial endocarditis, 251
 myopia caused by, 310
 skin lesions, generalized, caused by, 213
 therapy,
 dermatoses, 342
 pneumococcal infection, 342
 pneumonia, 431
 pneumonia, lobar, 353, 354
 poliomyelitis, 356
 psittacosis, 361
 staphylococcal infection, 342
 tetanus, 407
 trachoma, 412
 thrombocytopenic purpura caused by, 343, 344
 toxic effects, 134, 213, 343

Sulphapyridine—*continued*
 treatment of, in,
 bacillary dysentery, 118
 bacterial endocarditis, 118
 cerebrospinal fever, 187
 glandular fever, 118
 gonorrhoea, 117, 237, 238
 granuloma, ulcerative, 239
 hypopyon corneal ulcer, 198
 influenzal meningitis, 305
 laryngo-tracheobronchitis, 281
 lung abscess, 290
 lupus erythematosus, 118
 lymphocytic leukaemia, 286
 meningitis, 304, 305
 ophthalmia neonatorum, 196
 pneumococcal meningitis, 304
 pneumonia, 177, 178
 pyogenic meningitis, 304, 305
 subacute bacterial endocarditis, 251
 tetanus, 118
 tuberculosis, 415
 urinary tract complications due to, 346
 Sulphathiazole, 6
 agranulocytosis caused by, 134
 antiseptic snuff, as, 331
 clinical applications, 116
 effect on rigors in malaria therapy, 301
 general action, 340
 gonorrhoea treated by, 107
 haematuria caused by, 240
 local application of, 114, 115
 osteomyelitis and pericarditis treated by, 49
 renal complications, 343
 sodium salt of, in treatment of chronic sinusitis, 127
 therapy,
 osteomyelitis of spine, 397
 pneumonia, lobar, 352, 353, 354
 staphylococcal infection, 342
 urinary infections, 344, 345
 toxic effects, 134, 238, 240
 administration of *p*-aminobenzoic acid, 344
 treatment of, in,
 bacterial endocarditis, 118
 boils and carbuncles, 171
 cerebrospinal fever, 187
 diarrhoea, infantile, 208
 gonorrhoea, 237, 238
 toxic effects, 238
 pneumonia, 177
 urinary tract complications due to, 346
 Sulphonamides, 6, 114
 absorption, excretion, and distribution, 340
 anuria complicating therapy, 108
 B. coli infections treated by, 100
 bubonic plague treated by, 99
 cerebrospinal fever treated by, 65
 children's diseases treated by, 48
 clinical applications, 116
 cutaneous eruptions caused by, 344
 cyanosis resulting from, 115
 dosage and tolerance in child, 48
 dysentery treated by, 65
 excretion, 116
 glycerin-sulphonamide paste in burns, 182
 gonorrhoea treated by, 107, 108
 haematuria and renal colic due to, 116

INDEX

- Sulphonamides—*continued*
 internal use in septicaemias, 115
 leukaemoid reactions due to, 285
 local application of, 114, 115
 peritonitis, in, 13
 wounds, in, 266
 lymphogranuloma inguinale treated by, 109
 meningitis treated by, 58
 new compounds, 119
 ointments, 115
 otitis media treated by, 57
 otology and laryngology, in, 56
 pharmacology, 115, 340
 pneumococcus, effect on metabolism of, 342
 poliomyelitis treated by, 49
 powdered, in treatment of burns, 180
 rashes caused by, 344
 relative toxic effects, 116
 rheumatic fever treated by, 49
 septicaemia treated by, 58
 sodium compounds, 340
 urinary tract complications due to, 346
 sulphur-containing substances and, 346
 therapy,
 anuria complicating, 108
 cavernous sinus thrombophlebitis, 408
 ophthalmology, in, 342
 pneumococcal infection, 342
 pneumonia, lobar, 352
 puerperal sepsis, 370
 tracheo-bronchitis, 412
 trachoma, 412
 tropical diseases, 344
 thrombosis, septic, treated by, 59
 tonsillitis, acute, treated by, 60
 toxic effects, 6, 115, 116, 310, 343
 childhood, 48
 treatment of, in,
 abortion, incomplete, 126
 actinomycosis, 118, 129
 aural infections, 118
 bacillary dysentery, 118
 bacterial endocarditis, 118
 gonorrhoea, 117
 hypopyon corneal ulcer, 198
 lupus erythematosus, 118, 299
 lymphopathia venereum, 300
 ocular infections, 118
 pneumococcal meningitis, 304
 pneumonia, of, 177
 septicaemias, 115
 ulcerative colitis, 194
 wounds, 114, 115
 wounds, infected, 265, 266
 tropical diseases treated by, 99
 undulant fever treated by, 100
 urinary antiseptics, as, 117
 war wounds treated with, 10, 11
 Sulphonated oil, detergent in dermatitis venenata, as, 203
 Sulphur, containing substances and sulphonamides, 346
 Sulphydryl compounds, effect on wound healing, 113
 Supradiaphragmatic splanchnectomy, essential hypertension, in, 164
 Supraspinatus tendon, calcification in, 189
 Suprasternal bones, 371
 Supravital staining of leucocytes, 7
 Suramin, 112
 Surgery
 advances in, 8
 aged, of the, 380
 air-raid casualties, of, 265
 plastic, 12
 reparative or restorative, 12
 warfare, of, 8
 Suture
 coagulated blood plasma in nerve, 264
 silk, in infected wounds, 266
 synthetic plastic, 264
 Sympathectomy, cervico-thoracic, for acrocyanosis, 226
 Sympathomimetic and parasympathomimetic drugs, intravenous drip administration, 346
 Synapoidin, 22
 Syndrome
 Adams-Stokes, 246
 Banti's, 398
 crush, 9, 269
 injury, 1
 Da Costa's, 2, 244, 245
 effort, 2, 46, 244, 245
 Ehlers-Danlos, 230
 Guillain-Barré, 315
 Hand-Schüller-Christian. *See* Schüller-Christian, *infra*
 Korsakow's, 369
 Laurence-Moore-Biedl, 162, 351
 Löffler's, 157
 Marchiafava-Micheli, 140
 Ménière's, 422
 nephrotic, with hypertension, in diabetes mellitus, 205
 Parinaud's oculo-glandular, 109
 Paterson's, 128
 Plummer-Vinson, 128
 Rendu-Osler, 223
 scalenus, 189
 Schüller-Christian, 287
 Simmonds's, 390
 sprue, 26
 Waterhouse-Friderichsen, 132, 186
 Synovial membrane
 granuloma, traumatic, 274
 knee, of, glomus tumour, 393
 synovioma, malignant, 274
 tumours, 274
 Synovioma, malignant, 274
 Syntroge, peptic ulcer treated by, 327
 Syntropan, Parkinsonism treated by, 220
 Syphilide, nodular, of face, 403
 Syphilis, 102, 403
 acquired, 403
 aetiology, 403
 aneurysm caused by, 143
 aortic valvular change due to, 249
 blood, cytology of, 102
 congenital, 403
 heart disease, incidence of, 403
 Parrot's pseudo-paralysis, 404
 rhagades, 403
 unusual manifestations, 404
 conjugal neurosyphilis, 403
 diagnosis, 102
 extragenital infection, 403
 gastric, 234

INDEX

Syphilis—*continued*

- infectivity and age of infection, 102
- infectivity of vaginal and uterine secretions, 102
- intracranial, 315
- Kahn test, 103
- nodular syphilide of face, 403
- old age, in, incidence of, 380
- petechial haemorrhages caused by anti-syphilitic therapy, 405
- prognosis, 104
- pyrexia, artificial, in, 105
- resistance to infection with other organisms, 104
- secondary, 403
- serum tests, 103
- skin lesions resembling psoriasis, 403
- stomach, of, 234
- tertiary, 403
- treatment, 104, 404
 - acetarsone, 404
 - acetylglycarsenobenzene, 404
 - arsenical compounds, 105, 106, 404
 - arsenoxide, 105
 - bismuth, elimination of tissue deposits by ammonium chloride, 404
 - effect of thiosulphate on excretion of arsenic, 404
 - five-day treatment, 104
 - heat, by, 105
 - mapharside, 404
 - mercury, healing of obstructive lesions, 404
 - side effects, 405

T

- T.A.B.C. vaccine, 261
- Tachycardia, paroxysmal, symptoms, 150
- Tannic acid, burns treated with, 179, 181
- Tarsus, tuberculous, treatment of, 274
- Tattoo, mercury sulphide, for leucoplakia vulvae, 430
- Teeth
 - estimation of age from, 303
 - extraction, neurological complications, 202
 - Hutchinson's, in non-syphilitics, 202
 - hyperparathyroidism, in, 322
- Telangiectasia
 - familial haemorrhagic, associated haemorrhages, 223
 - hereditary, with visceral involvement, 223
- Temperature, low, cancer treated by, 184
- Temporal
 - artery,
 - inflammation of, 152
 - thrombosis of, 152
 - bone, Schüller-Christian syndrome involving, 287
- Temporal arteritis, 152
- Tendon
 - injuries of, 265
 - supraspinatus, calcification in, 189
- Teratoma, testis, of, concurrent seminoma, 405
- Test
 - collargol, 188
 - Dick, 261
 - exercise tolerance, 44, 244
 - flying aptitude, 29

Test—*continued*

- hydrochloric acid and collargol, 188
- Kahn, 103
- liver function, 4
- Mantoux, 292
- Meinicke flocculation, 414
- Paul-Bunnell, 235
- phenolphthalein, 273
- pulse response, 244
- Rorschach, 85
- Schick, 209
- Schumm's, 170
- secretin, 322
- tuberculin patch, 292
- visual capacity of aviators, 30, 31
- vitamin A absorption, 192
- Wesselow and Griffiths', 206
- Widal, 63
- Woldman, 273
- Testicles undescended, hormone treatment of, 5
- Testicular biopsy, diagnosis of sterility, in, 399
- Testis
 - abdominal, seminoma of, 405
 - absence of, 231
 - bilharziasis of, 405
 - diseases, 405
 - hydrocele, injection treatment, 406
 - interstitial celled tumour and precocity, 405
 - seminoma,
 - abdominal testis, of, 405
 - teratoma, and, 405
 - traumatic displacement causing, 405
 - traumatic displacement resulting in seminoma, 405
 - tumours, 405
 - undescended,
 - treatment, 406
 - chorionic gonadotrophic hormone and testosterone propionate, 406
 - gonadotrophic hormone, 406
 - surgical and hormonal, 406
- Testosterone
 - blood pressure, effect on, 382
 - eunuchism and hypogonadism treated by, 384, 385
 - inunction in chronic mastitis, 175
 - propionate,
 - effects of small doses on sex organs of rats, 384
 - endometriosis treated by, 221
 - eunuchism and hypogonadism treated by, 384, 385
 - impotence treated by, 261
 - prostatic hypertrophy treated by, 360
 - undescended testis treated by, 406
 - uterine bleeding, in, 21
- Tetanus, 406
 - combined immunization against tetanus and enteric fever, 407
 - following induced abortion, 126
 - immunization against diphtheria and, 260
 - prophylaxis, 407
 - toxoid, 407
 - treatment, 407
 - intracisternal injection of antitoxin, 407
 - sedation, antitoxin, and hexamine, 407
 - sulphapyridine and evipan sodium, 407

INDEX

- Trichinella spiralis*, isolation of larvae from arterial blood, 413
- Trichiniasis, 412
cerebral symptoms, 90
outbreaks in England, 413
- Tricho-epithelioma, 393
- Trichomonas vaginalis*
infestation, 429
infestation of male genito-urinary tract, 417
treatment, 429
- Tricresyl phosphate, poisoning by, 315
- Trigeminal neuralgia, 314. *See* Neuralgia, trigeminal
- Tropical
diseases,
chemotherapy in, 99
sulphonamides in, 344
medicine, 96
ulcer, whale-oil application, 413
- Trypanosomiasis
diamidines in, 100
treatment, 4 : 4'-diamidinostilbene, 413
- Tryparsamide
neurosyphilis treated by, 316
toxicity, 317
treatment of optic atrophy, in, 162
trypanosomes, effect on, 332
- Tubal pregnancy, 228
aetiology, 228
differential diagnosis, 228
pre-existing tubal infection, 228
- Tube, Miller-Abbott, 272
- Tubercle endotoxoid
Grasset's, in treatment of leprosy, 284
Grasset's, lupus vulgaris treated by, 300
- Tuberculo-silicosis, X-ray findings in, 390
- Tuberculoid, leprosy, 283
- Tuberculosis, 414
blood viscosity, 414
carriers, unsuspected, 414
diagnosis, 414
epidemiology, 414
erythema nodosum associated with, 224
experimental, effect of promin on, 336
immunity and allergy, 414
incidence of, 4
intestinal, 273
irido-cyclitis, 420
joints, of, 274
mediastinum, of, 302
Meinicke flocculation test, 414
prevention, 415
prognosis, 414
prostate, of, 359
pulmonary, 77
cavities, physics and pathology of, 77
clinical picture, 291
cor pulmonale, chronic, and, 291
course and prognosis, 292
diabetes mellitus associated with, 205
zinc protamine insulin in, 206
diagnosis and differential diagnosis, 292
eosinophilia in, 291
extension after operations, 292
gastric lavage, 292
gastro-intestinal complications, 292
Mantoux test, 292
mass radiography, 75, 76, 292
morbid anatomy and pathology, 291
- Tuberculosis—*continued*
pulmonary—*continued*
mortality rate, 291
pleuritic effusion, eosinophilia in, 291
post-operative complication, 292
screen photography, advantages of, 76
social factors, 291
sputum examination, 292
treatment, 292
hemi-diaphragmatic paralysis, 292
insulin and high carbohydrate dietary, 293
paraffin pack, 293
phrenic paralysis, 292
pneumothorax, artificial, 293
social administration and colonization, 292
tuberculin patch test, 292
uterine tuberculosis associated with, 22
X-ray examination, 292
spine, of, 396
susceptibility of red-haired persons, 414
tonsils, of, 408
treatment, 415
cod-liver oil, 415
sulphapyridine, 415
various local lesions, of, 415
vitamin C, 415
- Tuberculous
ankle, 274
duodenal ulcer, perforation of, 326
infections, promin in treatment, 119
obstructive emphysema in children, 219
pleuritic effusion, 291
tarsus, 274
tonsillitis, 408
ulceration, in gastro-intestinal tract, 273
ulcers of stomach, 401
- Tularaemia
bacteriology and morbid anatomy, 415
diagnosis from meningitis, 415
intracellular parasitism, 415
- Tulle gras dressings, 263
- Tumours
effect of irradiation on mitosis, 416
effects of oestrogen and androgen on cancer tissue, 183
giant-celled, of bone, 172
multinucleosis among Bantus, 416
radio-sensitivity of, 372
uniovular and binovular twins, in, 254
- Twins
identical, coeliac disease in, 191
tumours in uniovular and binovular, 254
- Typhoid fever
nutrition in, 221
treatment,
bananas, 221
sulphaguanidine, 222
- Typhus fever, 98, 99
epidemic or louse-borne, Mexican murine vaccination, 416

U

- Ulcer
gastro-jejunal, 328
tropical, whale-oil application in, 413

INDEX

- Ulceration
 decubital, of pharynx, 350
 jaws, of, non-malignant, 308
 lepromatous, 284
 phagedaenic, 392
 radionecrotic, zinc treatment, 372
 simple, of caecum, colon, and rectum, 193
 tuberculous,
 duodenum, of, 326
 gastro-intestinal tract, of, 273
 stomach, of, 401
 Ultra-violet irradiation
 air in hospitals, of, 130
 carcinogenic effect, 129
 effect on immunity, 260
 treatment of post-irradiation necrosis, in, 130
 Umbilical cord
 hernia in, 255
 prolapse of, 278
 Undulant fever, 416
 sulphonamides in treatment, 100
 Uraemia
 acute, polycystic disease of kidneys causing, 275
 treatment with desoxycorticosterone acetate, 417
 Ureter
 accidental bilateral ligation of, 276
 calculus. *See* Calculus, ureteral
 carcinoma,
 clinical picture, 277
 metastatic, 278, 361
 nephro-ureterectomy for, 277
 surgical injuries, 418
 Ureterocele, 231
 Urethane, quinine and, 112
 Urethra
 congenital obstruction, danger of infection in, 418
 diseases, 417
 female, congenital stricture, 418
 male,
 anomalies, 417
 congenital hypertrophy of verumontanum, 417
 inflammations, 417
 trichomonas vaginalis infestation, 417
 Urethritis, nearsphenamine treatment, 417
 Urinary
 antiseptics, sulphonamides as, 117
 tract,
 anomalies, in relation to chronic pyuria, 231
 complications due to sulphonamides, 346
 congenital obstruction and urinary infection, 418
 infection,
 congenital obstruction and, 418
 sulphanilamide in, 344, 345
 sulphathiazole in, 344, 345
 Urine
 alcohol in, estimation of, 134
 examination, 418
 pregnanediol in, 357
 retention,
 spinal anaesthesia, after, 162
 treatment by β -methylcholine urethane, 161
 Urogenital organs, abnormalities, 418
 Urography, excretion, 372
 Uroselectan B
 excretion pyelography, in, 371
 induction of labour by, 19
 thrombosis of injected veins, 371
 Uterine muscle, effect of raspberry-leaf extract on, 20
 Uterus
 carcinoma,
 cervix,
 endometriosis associated with, 419
 radium and X-ray therapy, 419
 treatment by local refrigeration, 419
 cobra venom for relief of pain, 419
 secondary growth in Fallopian tubes, 228
 contractions, and dysmenorrhoea, 214
 diseases and disorders, 419
 fibromyomas,
 irradiational treatment, 419
 prevention after oestrogen injections, 383
 haemangioma, X-ray therapy, 419
 haemorrhage,
 oestrogens in, 21
 testosterone propionate in, 21
 hydatid cyst, 419
 post-partum, effect of stilboestrol on, 370
 tuberculosis, pulmonary tuberculosis associated with, 22
 tumours, 419
 Uveal tract
 diseases, 420
 inflammation, 420
 sarcoma, prognosis of, 420
 Uveo-parotitis, 420
- V
- Vaccines
 enteric fevers, 261
 general paralysis of insane, in, 315
 Mexican murine typhus, 416
 prevention of colds, for, 193
 spray, intranasal, in prevention of colds, 193
 T.A.B.C., 261
 typhus fevers, epidemic, 416
 Vagina
 cysts and tumours, 430
 diphtheria, 429
 diseases, 429
 fistulae, 430
 hydrometrocolpos in infants, 430
 moniliasis of, 284
 trichomonas vaginalis infestation, 429
 vesico - vaginal fistulae, operation for, 430
 Vaginal
 fistulae, 430
 thrush, 284
 Vaginitis
 diphtheritic, 429
 monilial, and leucorrhoea, 284
 post-menopausal, treatment, 429
 senile, treatment of, 429
 trichomonas vaginalis causing, 429
 Vulvae conniventes, 27

INDEX

- Varicose veins—continued**
 retina in diabetic retinitis, of, 376
 sensitivity to sodium morrhuate and monoethanolamine oleate, 421
 significance of small intracutaneous veins on chest, 421
- Vascular**
 anastomosis, soluble rod method of, 264
 changes, associated with splenic disease, 397
 diseases, peripheral,
 action of vasodilator drugs, 151
 plethysmographic method of measuring blood-flow in, 151
- Vasoconstrictor**, shock treated by transfusion and, 388
- Vasodilators**, action in peripheral vascular diseases, 151
- Veins**
 diseases, 420
 obstruction, 420
 tumours, 422
 vertebral, 89
 wounds, 421
- Vena cava inferior**,
 leiomyosarcoma of, 422
 thrombosis of, 420
- Venereal diseases**, 102
 incidence, 102
 prophylaxis, 102
- Venom**, cobra, for relief of pain due to cancer, 184
- Venous**
 occlusion, effect on arterial flow to extremity, 151
 thrill, abdominal, in cirrhosis of liver, 288
 thrombosis, central nervous system, in, 92
- Ventricular**
 fibrillation, mechanism of, 150
 septum, transposition of great vessels with defect of, 248
- Ventriculography**, diagnosis of cerebral tumour, in, 175
- Veratrum viride**, therapy in eclampsia, 358
- Vertebrae**
 fourth lumbar, spondylolisthesis of, 161
 convulsion therapy causing, 80
- Vertebral veins**, 89
- Vertigo**, labyrinthine or aural, 422
- Verumontanum**, congenital hypertrophy of, 417
- Vesico-vaginal fistula**, operation for, 430
- Vincent's angina**, pharyngitis, acute, and, 349
- Virilism**, renal hypernephroma and, 133
- Virus**
 filter-passing,
 differentiation, in encephalitis epidemica, 220
 ecthyma contagiosum caused by, 217
 influenza, variation of strains in, 262
 influenza, 3
 yellow fever, cultivation of, 432
- Viscosimeter**, pipette type, 414
- Vision**
 aviators, of, 36
 effect of acute alcoholism on, 134
 night, 30, 31
 tests for, 31
- Vision—continued**
 stereoscopic, in relation to landing of aircraft, 31
- Visual capacity**, night flying, for, 30, 31
- Vitalium**, use in fixation of fractures, 210
- Vitamin A**, 5, 120
 absorption test in coeliac disease, 192
 deficiency,
 keratomalacia and, 209
 mineral oil laxatives and, 426
 obstructive hepatic jaundice, in, 273
 rheumatoid arthritis, in, 153
 miners' requirements, 426
 preferential solubility in mineral oil, 426
 quantitative requirements, 426
 therapy,
 Darier's disease, 200
 gastric ulcer, 327
 keratomalacia, 209
 keratosis follicularis, 200
 nephrosis, in, 313
- Vitamin B₁**, 5
 deficiency,
 alcoholic beri-beri and, 135
 multiple neuritis and hepatic cirrhosis, in, 289
 Wernicke's polio-encephalitis associated with, 369
 therapy,
 arsenical peripheral neuritis, 410
 chorea, 189
 diabetes mellitus, in, 206
 lichen planus, 287
 pellagra, 324
- Vitamin B₂**, 5, 121
 deficiency, 422, 423
 associated with diabetes mellitus, 206, 422
 cardiovascular disturbances and, 423
 effect on growth of infants, 50
 pink disease treated by, 50
 therapy,
 diphtheria, 210
 dyspnoea, 254
 heart failure, 254
 trigeminal neuralgia, in, 314
- Vitamin B₆**,
 complex, choline as member of, 423
 deficiency, 424
 'sore mouth' and, 308
- Vitamin B₁₂**, 5, 423
 importance in human nutrition, 424
 pyridoxin, 423
 therapeutic applications, 424
 therapy,
 amyotrophic lateral sclerosis, 428
 muscular dystrophy, 428
 paralysis agitans, 322
- Vitamin C**, 5, 121
 deficiency, 425
 epileptics, in, 222
 effect on muscle response to histamine, 425
 effect on wound healing, 13
 excretion, in infantile diarrhoea, 208
 level in schoolboys, 425
 nutrition in diabetes, 425
 nutrition of children, in, 49
 requirement, in asthma, 157
 scurvy and, 425

INDEX

- Vitamin C—*continued*
therapy,
 diabetes mellitus, 206
 erythraemia, 225
 pellagra, 324
 tuberculosis, 415
 wound healing, relation to, 268, 425
- Vitamin D, 5
 deficiency, in obstructive hepatic jaundice, 273
 distribution after large doses, 426
- Vitamin E, 5, 121
 muscular dystrophies treated by, 50
 therapy,
 amyotrophic lateral sclerosis, 307, 428
 muscular dystrophies and myotonias, 426
 muscular dystrophy, 428
 neuro-muscular disorders, 426
 treatment of, in,
 fibrositis, 230
 muscular disease, 230
- Vitamin K, 5, 6, 122, 427
 deficiency,
 associated with idiopathic steatorrhoea, 192
 post-operative, in obstructive jaundice, 273
 haemorrhagic disease of new-born treated by, 50
 menaphthone, official preparation, 113
 plasma-prothrombin relation in pernicious anaemia, 139
 pre-operative administration, in obstructive jaundice, 273
 prothrombin level,
 effect on, 427
 labour, in, effect on, 428
 prothrombin time in new-born, effect on, 427
 synthetic, coeliac disease treated by, 192
 therapy,
 coeliac disease, 192
 labour, in, 428
 treatment of icterus gravis neonatorum, in, 141
- Vitamin P, 5, 122
 capillary fragility and permeability, effect on, 426
 deficiency, 425
 therapy,
 haemorrhagic deficiency disorders, 241
 psoriasis, 362
 purpura, 241
 treatment of purpura complicating measles, in, 302
- Vitamins, 5, 49, 120, 422
 deficiency,
 associated with diabetes mellitus, 206
 coeliac disease, in, 192
 diarrhoea, chronic, causing, 208
 multiple neuritis and hepatic cirrhosis, in, 289
 pellagra-like condition in diabetes mellitus, 206
 fat soluble, 426
 hypovitaminosis of, in coeliac disease, 192
 therapy, diabetes mellitus, 206
 water-soluble, 422
- Voice, effect of helium-oxygen mixture on, 335
- Vomiting, winter, 232
- Vulva
 diseases, 429
 epithelioma, 430
 fusion, dangers of, 430
 leucoplakia, mercury sulphide tattoo, 430
 pruritus, use of stilboestrol cream, 430
 tumours, 430
- Vulvar fusion, 430
- Vulvo-vaginitis
 children, of, 108
 gonococcal, 108
- W
- War. *See also* Air-raids; Air-raid casualties; Aviation medicine; Flying; Soldiers; Recruits
 air-raid casualties, surgery of, 265
 blast injuries, 297
 burns, treatment of, 179
 drug shortage and, 111
 dyspepsia in armed forces, 214, 215
 epidemiological trends in, 62
 foot disease and military service, 232
 gastro-intestinal disease and, 214, 215
 heart disease and, 244, 245
 influenza in, 263
 malaria in war areas, 96
 mental disease, influence on, 363
 neuroses, 85, 86
 psychiatry, 85, 86
 psychoneurosis in, 85, 86, 363
 surgery, 8
 restorative or plastic, 12
 value of records in, 8
 tuberculosis, incidence of, 4
 wounds,
 chemotherapy of, 10, 11
 management of, 10
- Warts, plantar, X-rays and radium therapy, for, 393
- Waterhouse-Friderichsen syndrome, 132
 meningococcal septicaemia associated with, 186
- Wernicke's polio-encephalitis, vitamin B deficiency associated with, 369
- Wesselow and Griffiths' test, diabetes mellitus, in, 206
- Whale-oil, use in tropical ulcer, 413
- Wheat germ oil, lichen planus caused by, 286
- Whooping cough, 431
 complications and sequelae, 431
 diagnosis, 68
 pneumonia complicating, sulphapyridine therapy, 431
 prophylaxis, 69
 antigen, by, 431
 susceptibility, intracutaneous test, 431
 treatment, 68, 431
 antigen, 431
 intranasal soluble antigen, 431
- Widal test, 63
- Williams's apparatus for flying aptitude test, 29
- Wintergreen, oil of, fatal poisoning by, 409

INDEX

Winter vomiting, 232
 Woldman test, 273
 Woods, irritant, dermatitis caused by, 203
 Wound shock, 39. *See also* Shock
 Wounds, 263
 amnioplastin, use of, 264
 bacteriology of, 267
 chemotherapy of, 10, 11, 265
 closed plaster method, bacteriology of
 wounds treated by, 267
 dressings, 263, 264
 haemostasis, mechanism of, 268
 healing, 113
 nutrition, and, 13
 relation to vitamin C and serum protein,
 268
 rôle of vitamin C, 425
 infected, 265
 chemotherapy, 265
 early precautions, 266
 silk sutures in, 266
 treatment,
 closed plaster method, 267
 cystine hydrochloride, 268
 hypertonic sodium sulphate and acri-
 flavine solution, 268
 local use of sulphonamides, 266
 sulphonamides, 266
 zinc peroxide, 267
 local application of sulphonamides, 114,
 115
 petroleum jelly dressings, 264
 plaster of Paris casts, 'windowed' un-
 padded, 265
 serum protein concentration, 263
 sulphonamides as antiseptics, 114
 tulle gras dressings, 263
 war, management of, 10
 Wrist
 chromoblastomycosis on, 233
 fracture, 211

X

Xanthomatous biliary cirrhosis, 287
Xenopus laevis, 358
 Xenopus test, diagnosis of pregnancy, in, 358
 Xerostomia, nicotinic acid deficiency caus-
 ing, 424
 X-ray examination, 371
 air-raid casualties, 371
 aortic arch, right-sided, 246
 biliary dyskinesia, 233
 cerebral tumour, 175
 coeliac axis, calcification of, 153
 contrast media, 371
 coronary artery disease, 146
 Crohn's disease, 199
 cysticercosis, 200
 brain, of, 200
 dyspepsia in soldiers, 215
 foreign bodies, 371
 interauricular septum, defects of, 247
 intestinal obstruction, acute, 271
 kidney, 372
 labour, in, 280
 mass radiography, 75, 76, 292
 maxillary antrum, 127

X-ray examination—*continued*
 myelography with iodized oil, 371
 nervous system, 371
 peptic ulcer in soldiers, 215
 pleural effusions, 352
 Plummer-Vinson syndrome, 128
 pregnancy, in, 280
 prostate, 360
 pulmonary tuberculosis, in, 292
 pyelography. *See* Pyelography
 sinuses, nasal accessory, 127
 skeletal system, 371
 sodium thorium tartrate in, 371
 soft-tissue radiography in pregnancy, 280
 spinal cord, 371
 suprasternal bones, 371
 tuberculo-silicosis, 390
 uroselectan B in, 371
 X-ray therapy, 372
 blood, toxic effects on, 372
 bronchiogenic carcinoma, 374
 cancer, 372
 carcinoma,
 breast, of, 176
 cervix uteri, of, 373, 419
 skin, of, 394
 deep therapy, harmful effects on malignant
 bronchial tumour, 372
 ganglion, 243
 giant-celled tumour of bone, 172
 herpes zoster, 256
 high voltage, 373
 rheumatoid arthritis, 373
 intestine, small, effect on, 372
 Jensen's rat sarcoma, 372
 leukaemias, 'spray' technique in, 285
 myeloid sarcoma, 172
 osteoclastoma, 172
 plantar warts, 393
 pneumonia, lobar, 355
 psoriasis of nails, 362
 rectal carcinoma, 375
 serum cholesterol level, effect on, 372
 sinusitis, 127
 skin cancer, 394
 skin diseases, 373
 X-rays
 blood, toxic effects on, 372
 effect on mitosis, 416
 sarcoma, Jensen's rat, effect on, 372
 serum cholesterol level, effect on, 372
 skin, effect on, 373
 tumours, radio-sensitivity of, 372

Y

Yellow fever, 99
 virus, cultivation of, 432

Z

Zinc peroxide,
 radionecrotic ulcers treated by, 372
 use in surgical infections, 267
 Zinc protamine insulin
 diabetes mellitus, in, 206
 diabetes with tuberculosis, for, 206

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